

IN THE CLAIMS

1. (Currently Amended) A method of synthesis of a chemical compound having the formula A-B-C, wherein A is a chemiluminescent moiety comprising a phthalhydrazide, B is an energy acceptor moiety, and C is a biologically active moiety comprising a nucleophilic moiety, the method comprising the steps of either:

(a) (i) attaching a phthalhydrazide precursor to at least one aryl group of a diaryl ethylene to form a phthalhydrazide-precursor-ethylene conjugate;

(ii) condensing two phthalhydrazide-precursor-ethylene conjugates formed in step (a)(i) to form a phthalhydrazide-precursor-pentadiene conjugate;

(iii) converting the phthalhydrazide-precursor of the phthalhydrazide-precursor-pentadiene conjugate formed in step (a)(ii) to phthalhydrazide (A), thereby forming a carrier compound;

(iv) reacting the carrier compound formed in step (a)(iii) with a nucleophilic moiety of the biologically active moiety (C), thereby forming a chemical compound having the formula A-B-C, wherein A comprises phthalhydrazide, B comprises pentadiene and C comprises a biologically active moiety comprising a nucleophilic moiety; or

(b)(i) condensing two diaryl ethylenes each comprising a leaving group to form a pentadiene;

(ii) protecting the pentadiene formed in step (b)(i) by reaction with a nucleophile;

(iii) exposing the protected pentadiene formed in step (b)(ii) to a phthalhydrazide precursor, thereby displacing the leaving group and forming a protected phthalhydrazide-precursor-pentadiene conjugate;

(iv) converting the phthalhydrazide-precursor of the protected phthalhydrazide-precursor-pentadiene conjugate formed in step (b)(iii) to phthalhydrazide, thereby forming a protected carrier compound;

(v) hydrolyzing the pentadiene protecting group from the protected carrier compound formed in step (b)(iv), thereby forming an unprotected carrier compound; and

(vi) reacting the unprotected carrier compound formed in step (b)(v) with a nucleophilic moiety of the biologically active moiety (C), thereby forming a chemical compound having the formula A-B-C, wherein A comprises phthalhydrazide, B comprises pentadiene and C comprises a biologically active moiety comprising a nucleophilic moiety.

~~A method of synthesis of a chemical compound having the formula A-B-C~~

~~—where the A is a chemiluminescent moiety comprising a phthalhydrazide,~~

~~—B is an energy acceptor moiety, and~~

~~—C is a biologically active moiety~~

~~comprising the steps of~~

~~—— forming a benzophenone;~~

~~—— forming a diaryl ethylene; and~~

~~comprising the steps of at least one of~~

~~—— (a) forming benzophenone;~~

~~—— (b) forming a diaryl ethylene;~~

~~—— (c) attaching a precursor to generate a phthalhydrazide;~~

~~(d) condensing two ethylene precursor conjugates to form a precursor pentadiene conjugate;~~

~~(e) condensing two diaryl ethylene to form a pentadiene;~~

~~(f) attaching a precursor to a pentadiene to generate a phthalhydrazide, to form a precursor pentadiene conjugate; and~~

~~(g) converting a precursor to the phthalhydrazide by at least one of the corresponding reactions~~

~~—— phthalimide with hydrazine;~~

~~—— aminophthalic acid diester with hydrazine;~~

~~—— aminophthalic anhydride with hydrazine; and~~

~~—— hydrolysis of phthalhydrazide protected by a hydrolyzable group to form a carrier compound; and~~

~~—— reacting the carrier compound with the biologically active moiety to form a corresponding conjugate.~~

2. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein the compound serves to delivery the C moiety is designed for release to a desired biological compartment.

3. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein the compound is a prodrug.

4. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 3 wherein the compound serves as a prodrug for at least one of antiviral agents for the treatment of viral infections and anticancer agents for the treatment of cancers.

5. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 4 wherein the compound serves as a prodrug for the treatment of at least one of the group of viruses comprising Human Immunodeficiency Virus (HIV), herpes viruses such as Herpes Simplex Virus, (HSV),

Epstein-Barr Virus (EBV), Varicella Zoster (VZV), Cytomegalovirus (CMV), HSV-6, and HSV-8 (Kaposi's sarcoma), Human Papilloma Virus (HPV), rhinoviruses, and hepatitis-linked viruses.

6. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 4 wherein the compound serves as a prodrug for the treatment of at least one of the group of cancers comprising colon, breast, lung, renal, retinal, and skin.

7. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 3 wherein the prodrugs have increased bioavailability.

8. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 2 wherein the compound is a cellular permeant prodrug.

9. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 8 wherein intracellular drug release occurs when the prodrug reacts with cellular free radicals via a mechanism involving chemiluminescence, photochromism, and intramolecular energy transfer.

10. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein the C moiety is a pharmaceutical agent or drug.

11. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 10 wherein the pharmaceutical agent is at least one of the group of antilipidemic drugs, anticholesterol drugs, contraceptive agents, anticoagulants, anti-inflammatory agents, immuno-suppressive drugs, antiarrhythmic agents, antineoplastic drugs, antihypertensive drugs, epinephrine blocking agents, cardiac inotropic drugs, antidepressant drugs, diuretics, antifungal agents, antibacterial drugs, anxiolytic agents, sedatives, muscle relaxants, anticonvulsants, agents for the treatment of ulcer disease, agents for the treatment of asthma and hypersensitivity reactions, antithrombotic agents, agents for the treatment of muscular dystrophy, agents to effect a therapeutic abortion, agents for the treatment of anemia, agents to improve allograft survival, agents for the treatment of disorders of purine metabolism, agents for the treatment of ischemic heart disease, agents for the treatment of opiate withdrawal, agents which activate the effects of secondary messenger inositol triphosphate, agents to block spinal reflexes, and antiviral agents including a drug for the treatment of AIDS.

12. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein the C moiety is released by an oxidation reduction reaction with the target cell's electron carriers or by

reaction with free radicals produced as a consequence of electron transport.

13. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 12 wherein the C moiety is released into a desired compartment in active form.

14. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 13 wherein the released C moiety has a greater therapeutic effect or therapeutic ratio relative to the free C agent alone.

15. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 14 wherein the released C moiety has a greater therapeutic effect or therapeutic ratio relative to the free C agent alone as a consequence of at least one of altered pharmacokinetics or pharmacodynamics such as a desirable kinetics of release, a resistance to inactivation or excretion, greater solubility, enhanced absorption, a diminished toxicity, or greater access to the cellular or biological compartment which is the site of action of C.

16. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein A represents a functionality which undergoes at least one of

an oxidation reduction reaction where electrons are transferred directly between A and the target cell's electron carriers, and

a reaction with free radicals of oxygen which are produced as a consequence of electron transport

such that an excited state is produced in A as a consequence of its participation in one of these reactions.

17. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 16 wherein A undergoes intramolecular energy transfer from its own excited state to the B functionality which is an energy acceptor.

18. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 17 wherein upon receiving energy from A, B achieves an excited state which relaxes through heterolytic cleavage of the covalent bond of B with C where C is a drug moiety which is released into the environment.

19. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 18 wherein the released drug molecule effects a therapeutic functional change by a mechanism which comprises

receptor mediated mechanisms including reversible and irreversible competitive agonism or antagonism including a molecule known as a suicide substrate or a transition state analogue mechanism or a noncompetitive or uncompetitive agonism or antagonism or the action is by a nonreceptor mediated mechanism including a "counterfeit incorporation-mechanism".

20. (Currently Amended) A method of synthesis of a chemical compound having the formula A-B-C

where A is a chemiluminescent moiety selected from the group consisting of phthalhydrazides, sulfonyloxamides and active oxalates;

B is an energy acceptor moiety~~[[,]]~~; and

C is a biologically active moiety comprising a nucleophilic moiety;

the method comprising the steps of condensing A and B to form conjugate A-B and reacting the conjugate A-B with C ~~wherein the chemiluminescent moiety comprises a molecule selected from the group consisting of~~

~~—— molecules undergoing reaction involving peroxides and oxygen free radicals,~~

~~—— molecules undergoing reaction involving oxidation or reduction, and~~

~~—— molecules undergoing both reaction with peroxides and oxygen free radicals followed by an oxidation or reduction reaction.~~

21-24. (Cancelled)

25. (Currently Amended) ~~The method of synthesis of the compound of~~ claim 20 wherein the energy acceptor moiety B is a photochromic compound.

26. (Currently Amended) ~~The method of synthesis of the compound of~~ claim 25 wherein the photochromic compound comprises one which demonstrate photochromic behavior with electromagnetic radiation and bleaching agents.

27. (Currently Amended) ~~The method of synthesis of the compound of~~ claim 26 wherein the A functionality is chemiluminescent, and the B functionality is such that the photodissociative drug release spectrum of B overlaps the chemiluminescence spectrum of A.

28. (Currently Amended) ~~The method of synthesis of the compound of~~ claim 25 wherein the photochromic compound comprises a cationic dye.

29. (Currently Amended) ~~The method of synthesis of the compound of~~ claim 28 wherein the

cationic dye comprises at least one of a di and triarylmethane dyes, triarylmethane lactones and cyclic ether dyes, cationic indoles, pyronines, phthaleins, oxazines, thiazines, acridines, phenazines, and anthocyanidins, and cationic polymethine dyes and azo and diazopolymethines, styryls, cyanines, hemicyanines, dialkylaminopolyenes, and other related dyes.

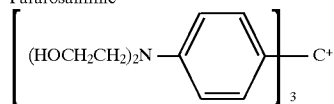
30. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 28 wherein the cationic dye comprises at least one of

Malachite Green	42000
Helvetia Green	42020
Basic Blue 1	42025
Brilliant Blue	
Setoglaurine	
Basic Green 1	42040
Brilliant Green	
Acid Blue 1	42045
Xylene Blue VS	
Patent Blue V	
Alphazurine 2G	
Acid Blue 3	42051
Brilliant Blue V	
Patent Blue V	
Food Green 3	42053
FDC Green 3	
Acid Green 6	42075
Light Green SF Bluish	
Acid Blue 7	42080
Xylene Blue AS	
Patent Blue A	
Acid Green 3	42085
Acid Blue 9	42090
Erioglaurine	
Acid Green 5	42095
Light Green SF Yellowish	
Acid Green 9	42100

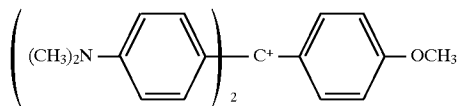
Erioviridene B	
Acid Blue 147	42135
Xylene Cyanol FF	
Basic Red 9	42500
Pararosaniline	
Basic Violet 14	42510
Fuchsin	
Magenta	
Basic Fuchsin	42510B
Basic Violet 2	42520
New Magenta	
Hoffman Violet	42530
Iodine Violet	
Basic Violet 1	42535
Methyl Violet	
Basic Violet 13	42536
Methyl Violet 6B	
Basic Violet 3	42555
Crystal Violet	
Gentian Violet	
Iodine Green	42556
Basic Blue 8	42563
Victoria Blue 4R	
Acid Blue 13	42571
Fast Acid Violet 10B	
Acid Blue 75	42576
Eriocyanine A	
Methyl Green	42585
Ethyl Green	42590
Basic Violet 4	42600
Ethyl Violet	
Acid Violet 49	42640
Wool Violet 5BN	
Acid Blue 15	42645
Brilliant Milling Blue B	
Acid Violet 17	42650

Acid Violet 6B	
Wood Violet 4BN	
Formyl Violet	
Acid Violet 5BS Conc.	
Acid Violet 19	42685
Acid Fuchsin	
Red Violet 5R	42690
Acid Blue 22	42755
Aniline Blue	
Soluble Blue	
Solvent Blue 3	42775
Solvent Blue 3	42780
Methyl Blue	
Aurin	43800
Mordant Blue 3	43820
Eriochrome Cyanine R	
Acid Green 16	44025
Naphthalene Green V	
Pontacyl Green NV Extra	
Basic Blue 11	44040
Victoria Blue R	
Basic Blue 15	44085
Night Blue	
Acid Green 50	44090
Wool Green S	
Kiton Green S. Conc.	
Basic Green 3	
Sevron Green B	
Brilliant Blue F & R Extra	
Brilliant Green Sulfonate	
Hexakis (hydroxyethyl)	

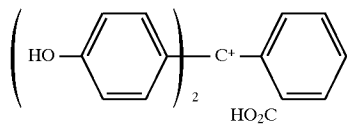
Pararosaniline



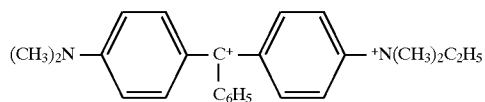
New Green



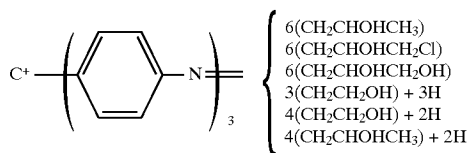
Phenolphthalein



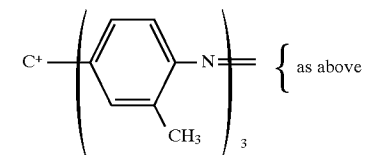
Malachite Green Ethiodide



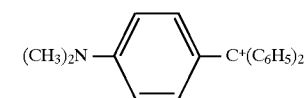
Hydroxyalkylated Pararosanilines



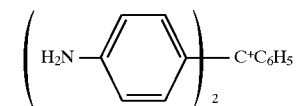
Hydroxyalkylated New Fuchsin



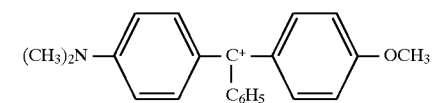
New Yellow



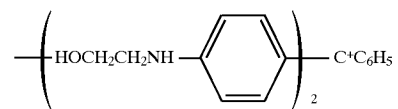
Doebner's Violet



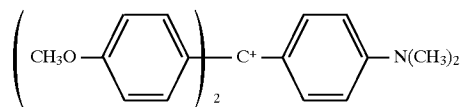
New Red



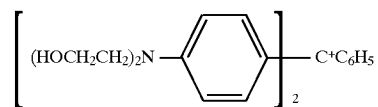
Bis(hydroxyethyl) Doebner's Violet



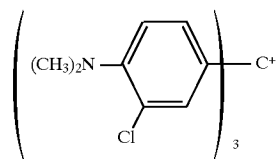
"New Magenta"



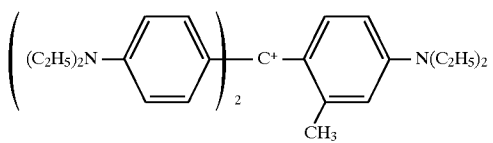
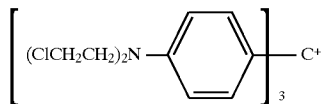
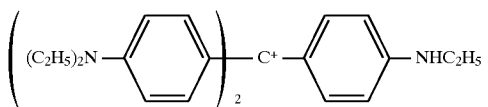
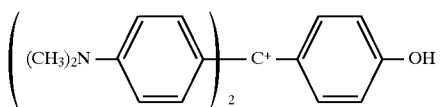
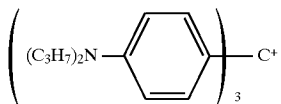
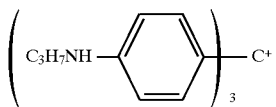
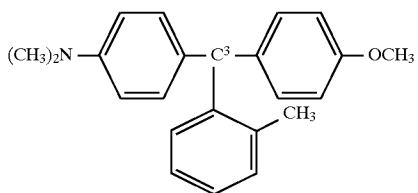
Tetrakis(hydroxyethyl) Doebner's Violet

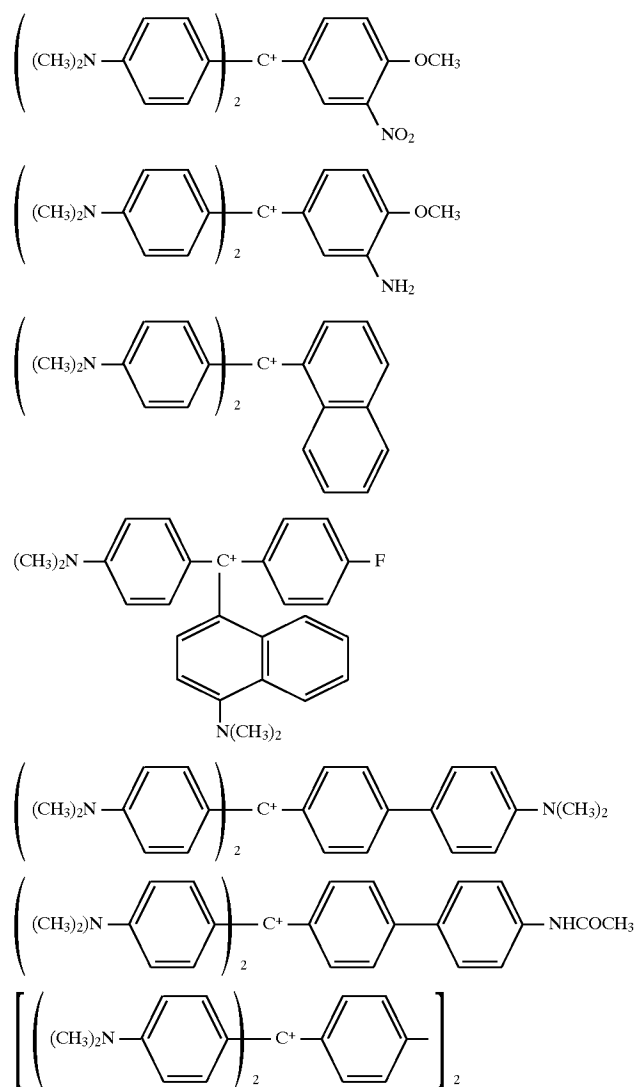


Trichloro Crystal Violet



Slow Red





^a Only the cyanide, bisulfite, and hydroxide ions are considered, regardless of the other anions present in the solution.

^b More detailed descriptions of the compositions of photochromic materials tested are given in Macnair's review [255; tables 1A-4].

^c Ethanol.

^d Diethyl ether.

^e 1,2-Dichloroethane.

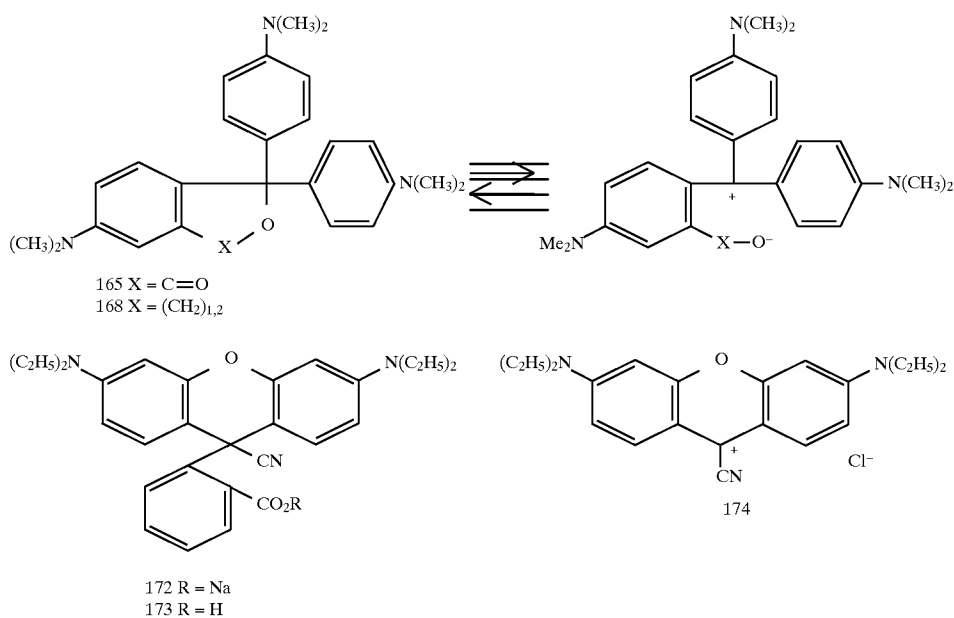
^f 1,1-Dichloroethane, cyclohexane-1,1-dichloroethane, or cyclohexane-1,2-dichloroethane mixtures.

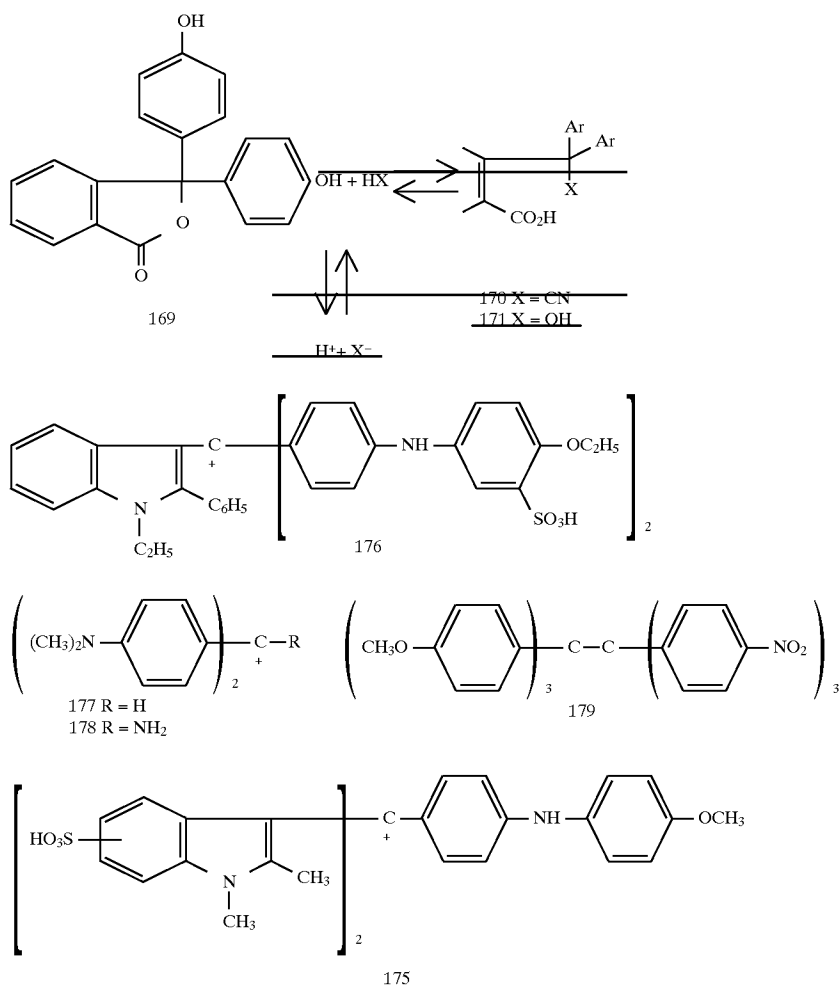
^g Benzene.

^h Dimethylsulfoxide, neat and aqueous.

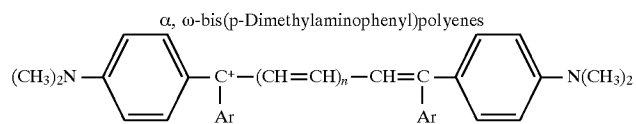
- ⁱ Acetone.
- ^j Acetic acid.
- ^k Ethyl acetate.
- ^l Ethyl bromide.
- ^m 2-Methoxyethanol.
- ⁿ Chloroform.
- ^o Ethanol with KCN.
- ^p Ethanol with KOH.
- ^q Carboxylic acids-acetic to stearic; hydrocinnamic acid; ethyl and butyl acid phthalates.
- ^r Octadecylnitrile, tributyl phosphate, aniline, 2-(p-tert-butylphenoxy)ethanol, tetraethyleneglycol dimethyl ether, or poly(ethylene glycols).
- ^s Amides-formamide to stearamide; methylformamide or methylacetamide; dimethyl- or diethyl-formamide or acetamide.
- ^t Three-to-one solutions of cellulose acetate with any of the following five-to-one plasticizer mixtures: butyl stearate, Polyethylene Glycol 600-butyl acetoxystearate, butyl stearate, or Dowanol EP-butyl acetoxystearate.
- ^u Water containing SO₂.
- ^v Water containing bisulfite and papain.
- ^w Poly(vinyl alcohol) with dimethylsulfoxide (5:1).
- ^x Films, containing residual solvent, cast from the following solutions: ethanol-acetone solutions of vinyl acetate-vinyl alcohol copolymer; aqueous poly(vinyl alcohol); aqueous poly(vinyl pyrrolidone); or aqueous methyl vinyl ether-maleic acid copolymer.
- ^y Methanol-dioxane with aqueous NH₄ HSO₃.
- ^z Paper impregnated with a toluene solution of poly(methyl methacrylate), stearic acid, and 2-(p-tert-butylphenoxy)ethanol, then dried.
- ^{aa} Intracellular impregnation of cellulose with the following swelling agents: n-propylamine, n-butylamine, n-hexylamine, 2-aminoethanol, dimethylformamide, acetic acid, dimethylsulfoxide, methylacetamide, dimethylacetamide, or formamide.
- ^{bb} Films cast from an approximately 4:3 mixture of a 20% solution and cellulose acetate butyrate in toluene-ethyl acetate (1:1) and triallylcyanurate in dioxane.
- ^{cc} Films cast from a 2:1 mixture of a 25% solution of cellulose acetate butyrate in toluene-ethyl acetate (1:1) and the titanium esters of N,N,N', N'-tetrakis(2-hydroxypropyl) ethylenediamine.
- ^{dd} Pure water.
- ^{ee} Films cast from aqueous gelatin or other hydrocolloids.
- ^{ff} Dimethylsulfoxide with methanolic KCN.
- ^{gg} 2-Methoxyethanol with methanolic KCN.

- ^{hh} Water or aqueous methanol containing bisulfite.
- ⁱⁱ Paper impregnated with m-dimethoxybenzene, acetonitrile, acetic acid, or phenyl methyl carbinol.
- ^{jj} Ethanol-benzene.
- ^{kk} Aqueous ethanol, methanol, aqueous methanol, aqueous acetone, benzene-methanol, carbon tetrachloride-methanol, cyclohexane-methanol, or chloroform-methanol.
- ^{ll} Films cast from 3:1 solutions of cellulose acetate and either Polyethylene Glycol 600 .RTM. or ethylene glycol phenyl ether as plasticizer.
- ^{mm} Films, containing residual solvent, cast from solutions of either cellulose acetate in 2-methoxyethanol or poly(vinyl alcohol) in aqueous ethanol.
- ⁿⁿ Films, containing residual solvent, cast from solutions of either cellulose acetate butyrate in 2-methoxyethanol or poly(vinyl acetate) in methanol.
- ^{oo} Ethanol containing ammonia.
- ^{pp} Aqueous methanol containing NH_4HSO_3 and urease.
- ^{qq} Aqueous methanol containing NH_4HSO_3 , with or without sodium dithionite.
- ^{rr} Aqueous acid at pH 1.
- ^{ss} Aqueous ammonia containing KCN.
- ^{tt} Paper impregnated with aqueous solutions with or without hydrocolloids.
- ^{uu} 2-Methoxyethanol containing HCl.
- ^{vv} Aqueous methanol containing NH_4HSO_3 , and glucose oxidase.
- ^{ww} 9:1 Methanol-water.
- ^{xx} Aqueous NaOH.





Photochromic Polymethine Dyes



Ar

n

C₆H₅

0, 1, 2

4-(CH₃)₂NC₆H₄

0, 1, 2

4-(CH₃)₂CHC₆H₄

0, 1, 2, 3, 4

4-CH₃OC₆H₄

0, 1, 2

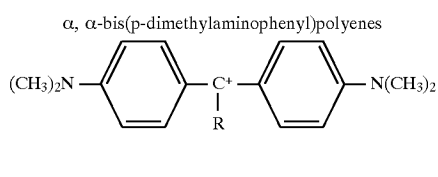
4-C₄H₉OC₆H₄

0, 1, 2

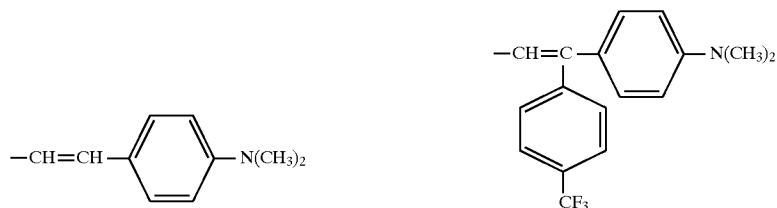
3-CH₃C₆H₄

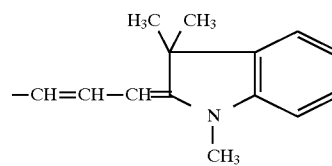
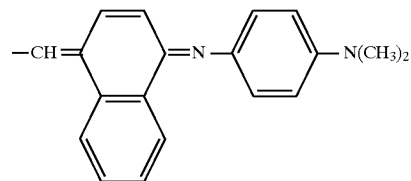
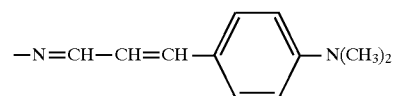
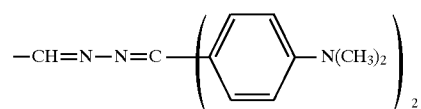
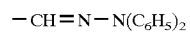
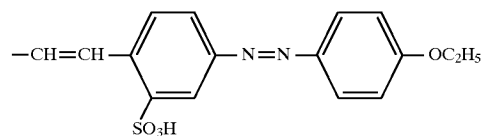
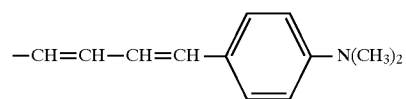
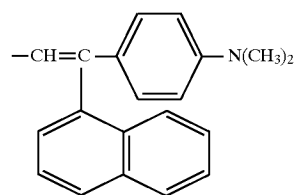
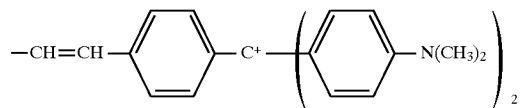
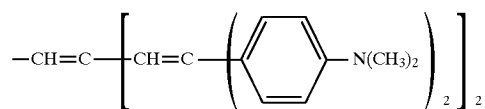
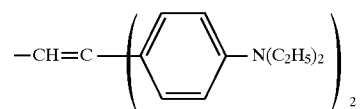
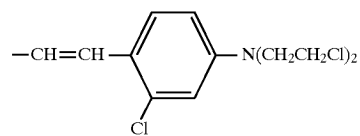
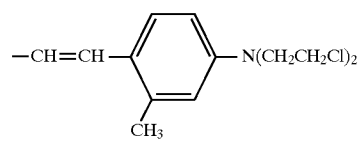
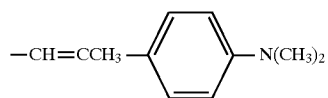
1, 2

4-t-C ₄ H ₉ C ₆ H ₄	1, 2
4-C ₂ H ₅ OC ₆ H ₄	1, 2
4-C ₃ H ₁₁ C ₆ H ₄	1, 2
4-FC ₆ H ₄	1
4-Fsub ₃ CC ₆ H ₄	1
2-(C ₆ H ₅) ₂ NC ₆ H ₄	1
3,4-H ₂ N(OCH ₃)C ₆ H ₃	1
2-Naphthyl	1, 2
4-ClC ₆ H ₄	2
2,4-Cl ₂ C ₆ H ₃	2
1-Naphthyl	2

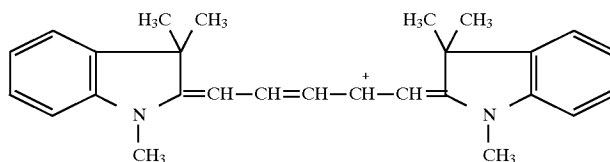
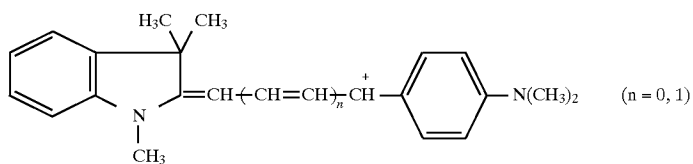
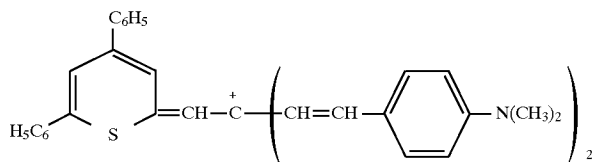
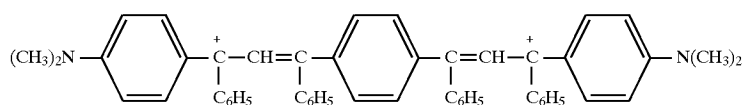
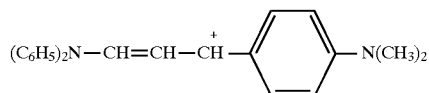
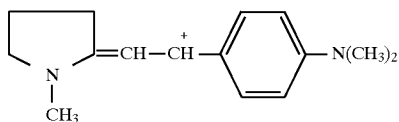
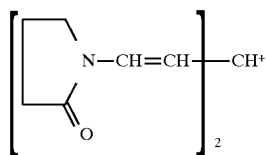


wherein each R comprises a functional group selected from the group consisting of alkyl, cycloalkyl, alkoxycarbonyl, cyano, carbamoyl, heterocyclic rings containing C, O, N, S, sulfo, sulfamoyl, alkoxysulfonyl, phosphono, hydroxyl, halogen, alkoxy, alkylthiol, acyloxy, aryl, alkenyl, aliphatic, acyl, carboxyl, amino, cyanoalkoxy, diazonium, carboxyalkylcarboxamido, alkenylthio, cyanoalkoxycarbonyl, carbamoylalkoxycarbonyl, alkoxy carbonylamino, cyanoalkylamino, alkoxycarbonylalkylamino, sulfoalkylamino, alkylsulfamoylalkylamino, oxido, hydroxy alkyl, carboxy alkylcarbonyloxy, cyanoalkyl, carboxyalkylthio, arylamino, heteroarylamino, alkoxycarbonyl, alkylcarbonyloxy, cyanoalkoxy, alkoxycarbonylalkoxy, carbamoylalkoxy, carbamoylalkyl carbonyloxy, sulfoalkoxy, nitro, alkoxyaryl, halogenaryl, amino aryl, alkylaminoaryl, tolyl, alkenylaryl, allylaryl, alkenyloxyaryl, allyloxyaryl, cyanoaryl, carbamoylaryl, carboxyaryl, alkoxycarbonylaryl, alkylcarbonyoxyaryl, sulfoaryl, alkoxysulfoaryl, sulfamoylaryl, and nitroaryl;

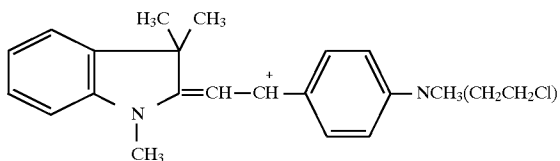




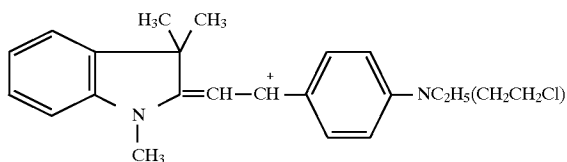
Miscellaneous Polyenes

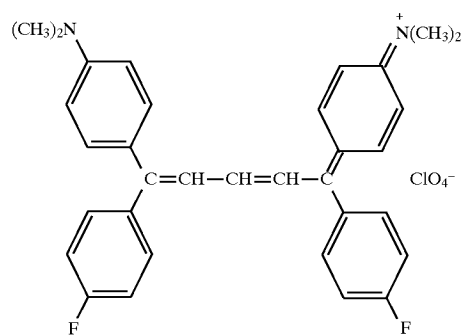
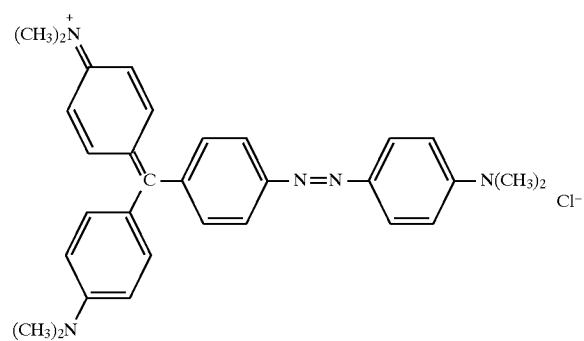
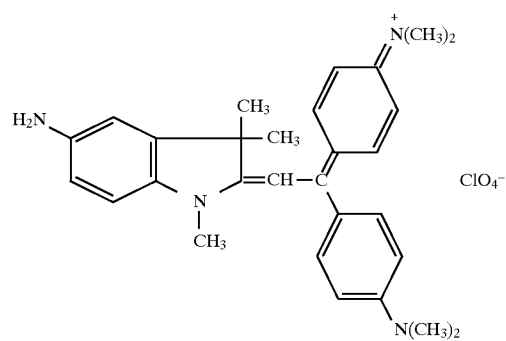
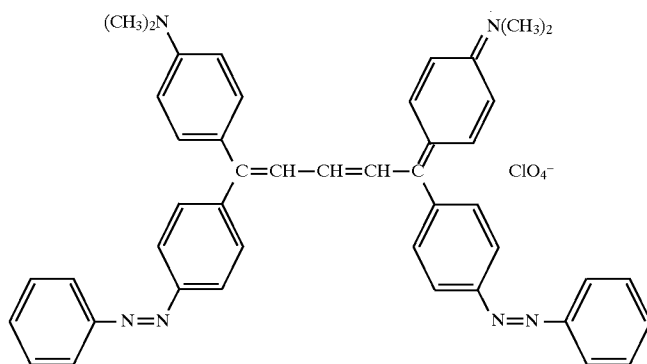


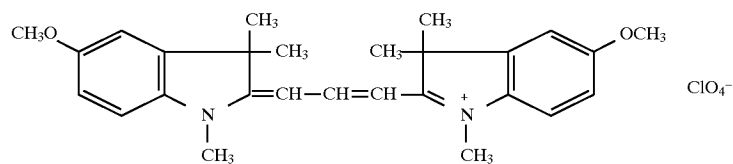
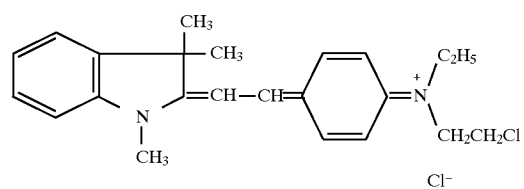
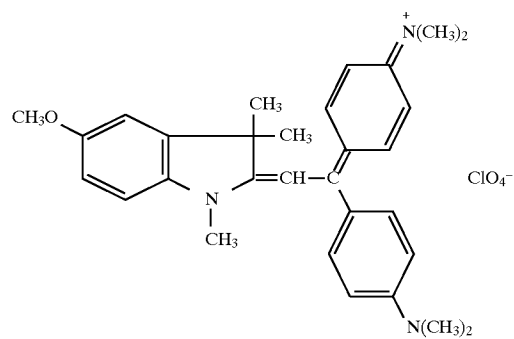
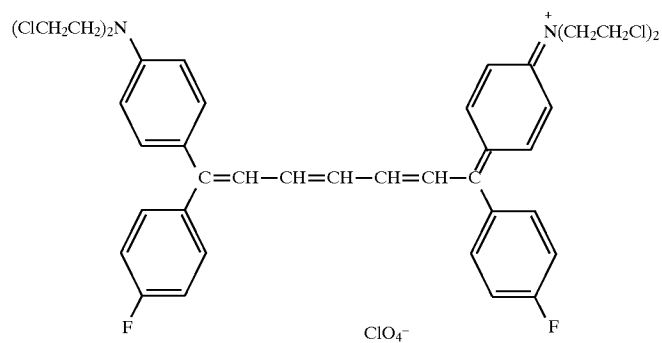
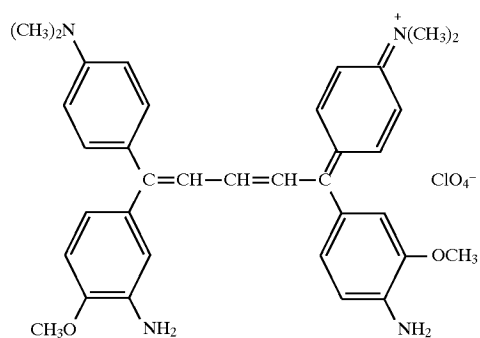
Basic Red 13

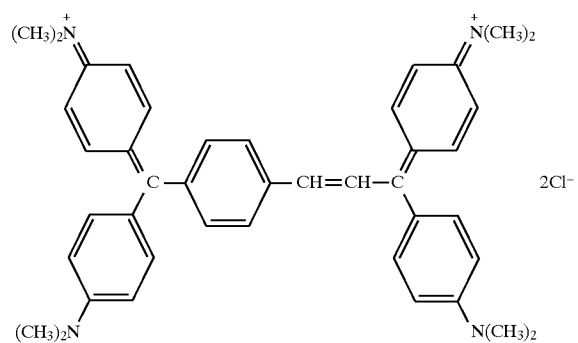
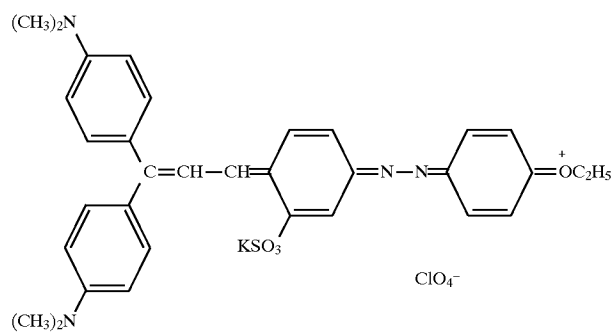
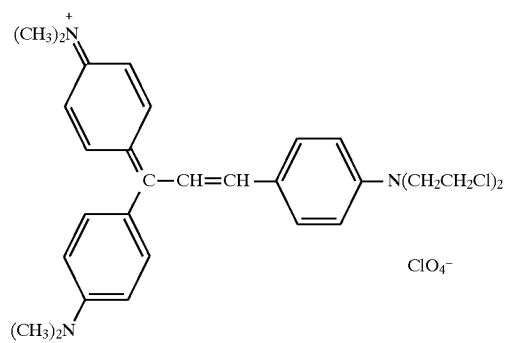
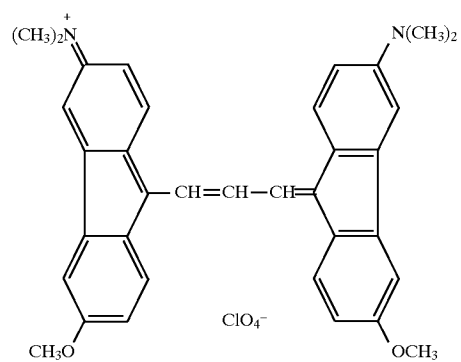


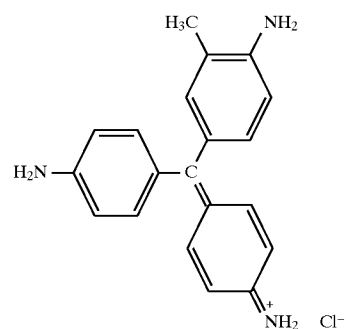
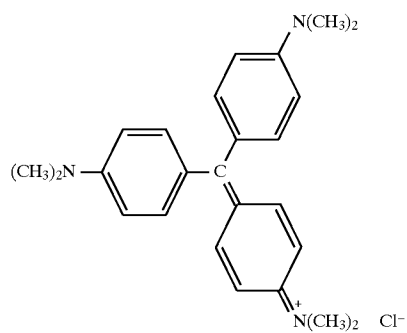
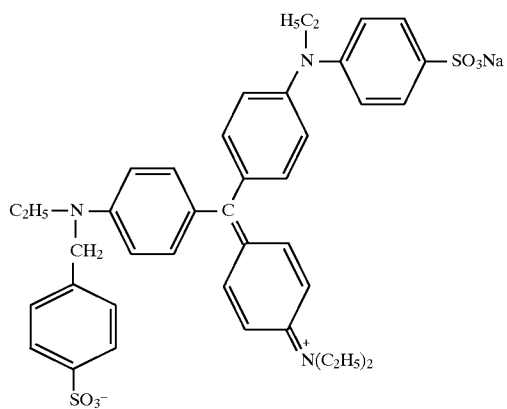
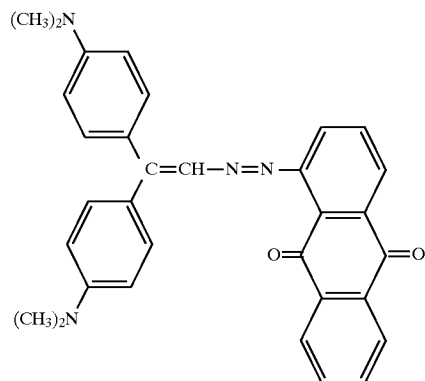
Basic Violet 7

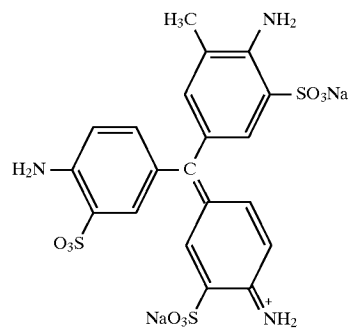
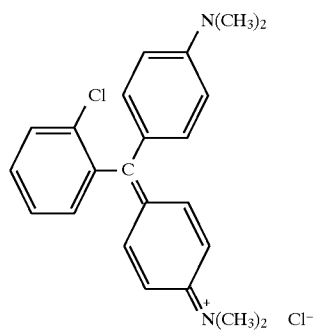
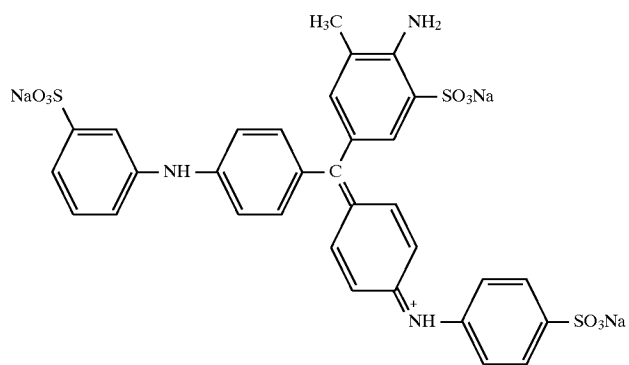
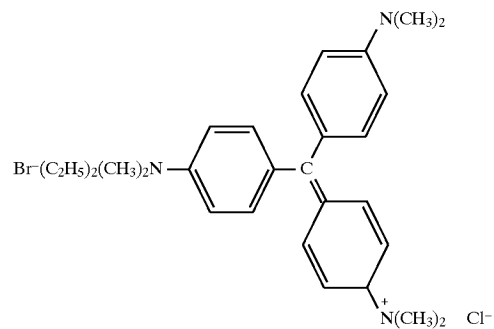
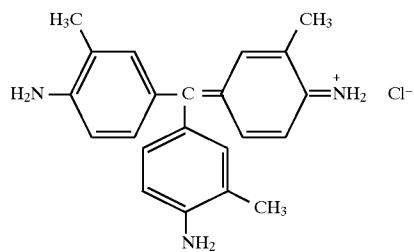
Basic Red 14
Basic Red 15
Basic Violet 15

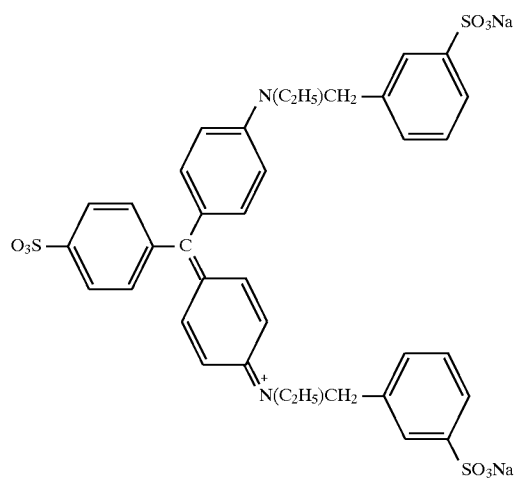
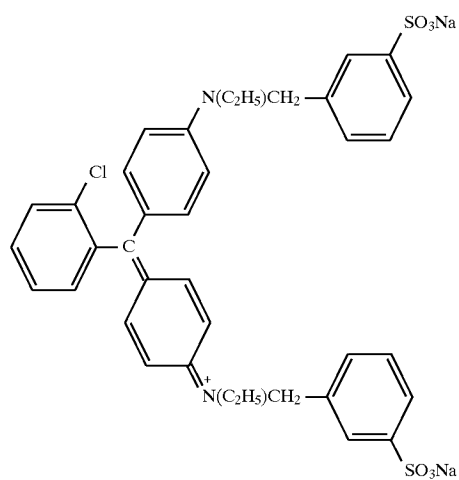
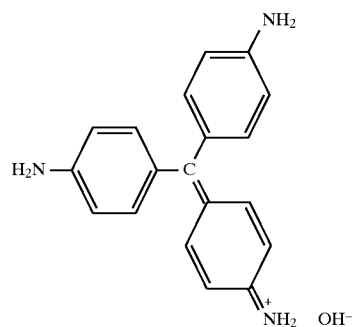
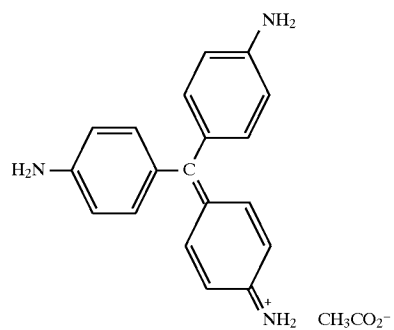


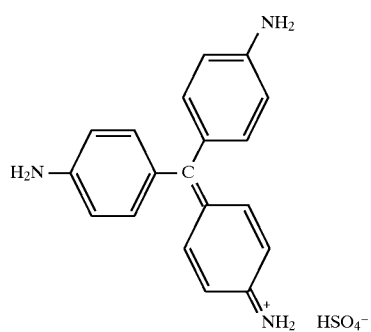
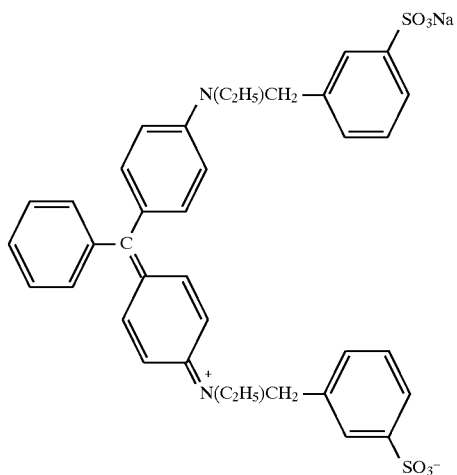






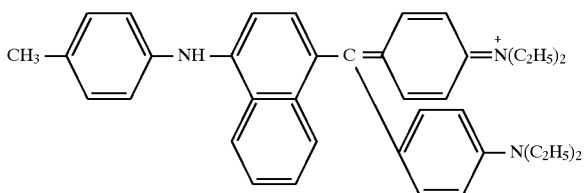




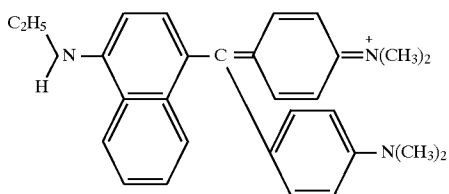


Salt-Isomerism Type Phototropic Dyes

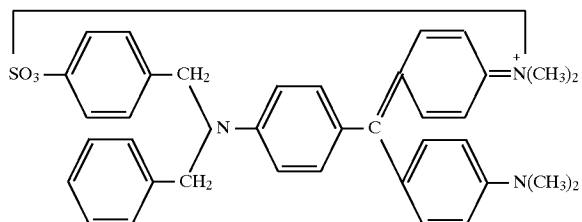
Night Blue



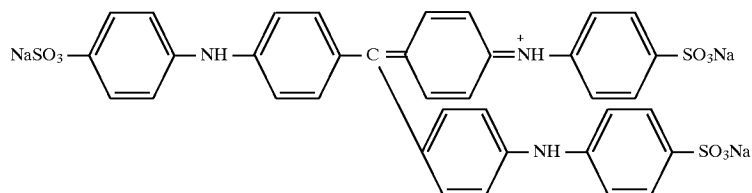
Victoria Blue R



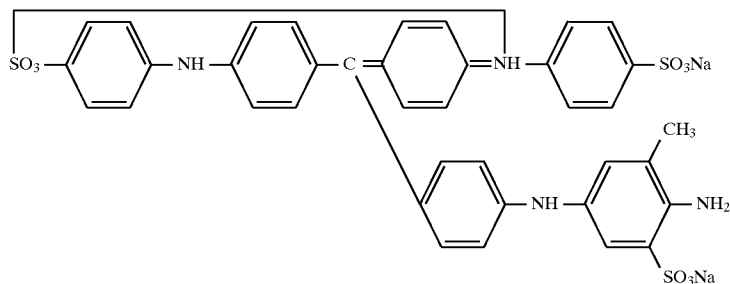
Brilliant Milling Blue B
Brilliant Blue F & R Ex.
Eriocyanine A



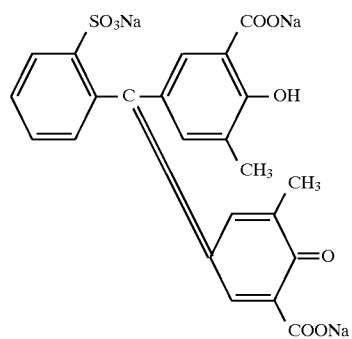
Methyl Blue



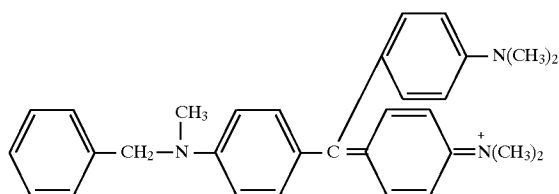
Aniline Blue



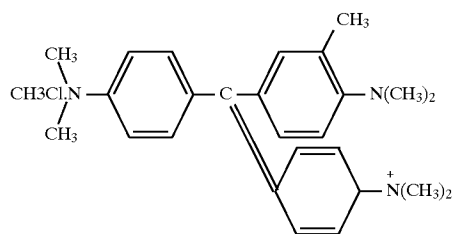
Eriochrome Cyanine R



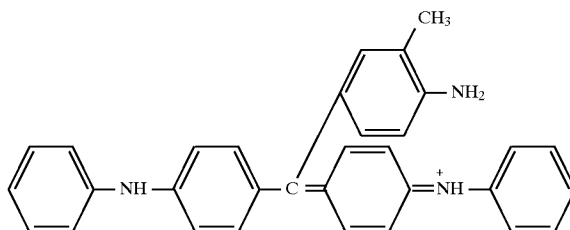
Methyl Violet 6B



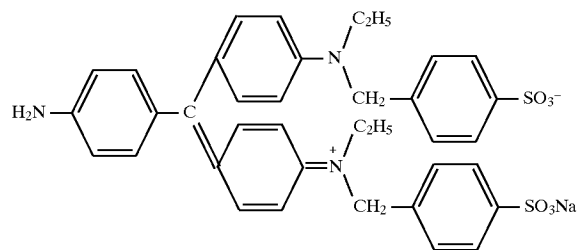
Iodine Green



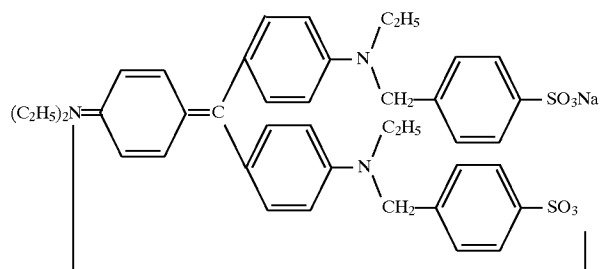
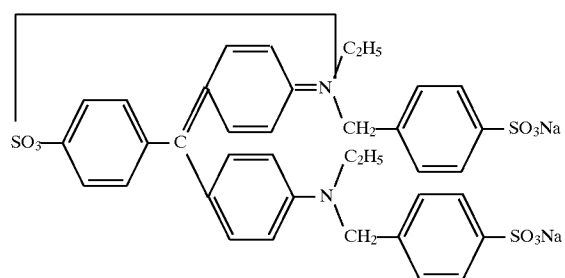
Aniline Blue



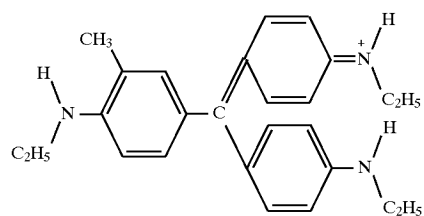
Wool Violet 5 BN



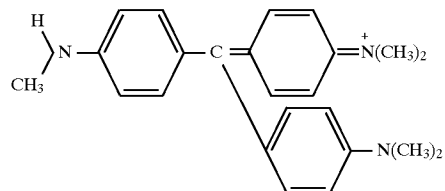
Wool Violet 4 EM

Light Green SF
Yellowish

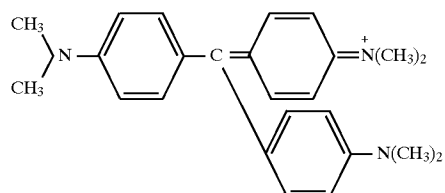
Iodine Violet



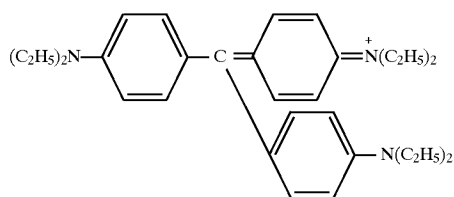
Methyl Violet



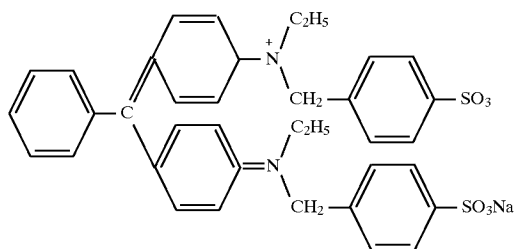
Crystal Violet



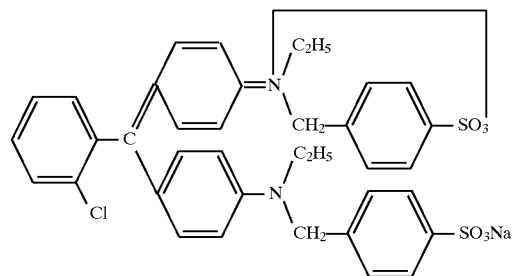
Ethyl Violet



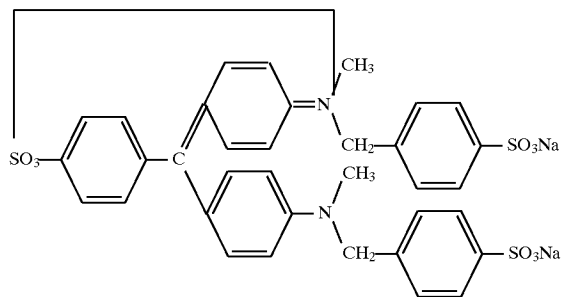
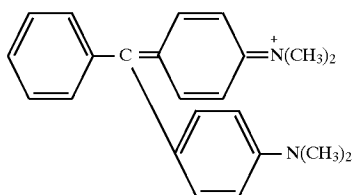
Acid Green L Extra



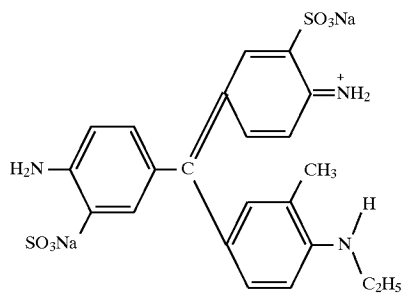
Erioviridene B



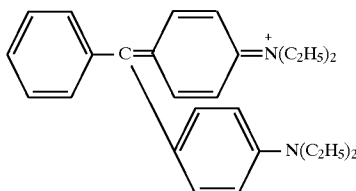
Light Green SF

Victoria Green
(Malachite Green)

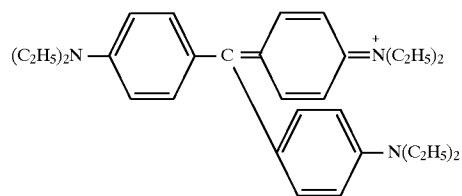
Red-Violet 5R



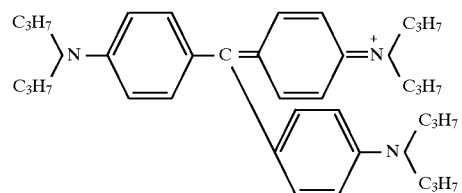
Brilliant Green "B"



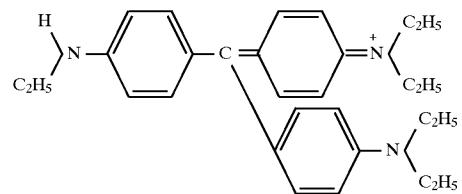
Di-[4(N,N-diethylamine)phenyl]-[4-(N,N-diethylamine-2-methyl) phenyl] methyl carbonium



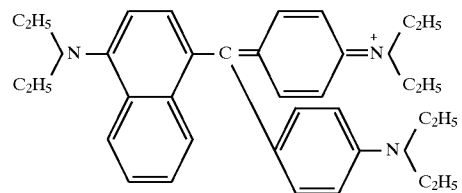
Tri-[4(N,N-dipropylamino)phenyl] methyl carbonium



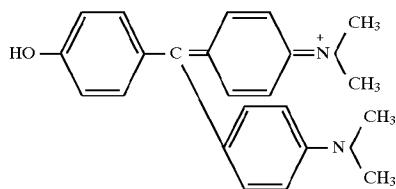
Di-[4(N,N-diethylamino)phenyl]-[4(ethylamino)-phenyl] methyl carbonium



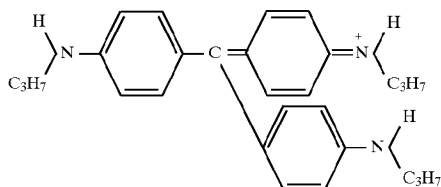
Di-[4(N,N-diethylamino)phenyl]-[4(N,N-diethylamino)naphthyl] methyl carbonium



Di-[4(N,N-dimethylamino)phenyl]-[4(hydroxy)phenyl]
methyl carbonium



Tri-[4(N-propylamino)phenyl] methyl carbonium

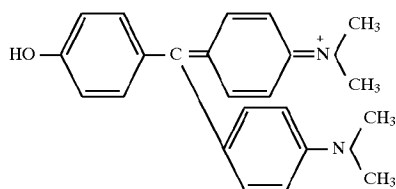


Hectolene Blue DS-1398

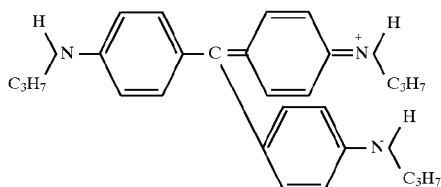
Hectolene Blue DS-1823

Sevron Brilliant Red 4G

Di-[4(N,N-dimethylamino)phenyl]-[4(hydroxy)phenyl]
methyl carbonium



Tri-[4(N-propylamino)phenyl] methyl carbonium



Hectolene Blue DS-1398

Hectolene Blue DS-1823

Sevron Brilliant Red 4G

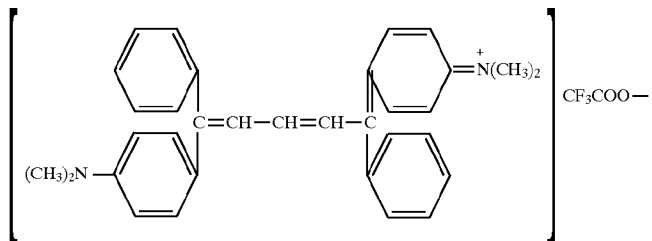
Genacryl Red 6B

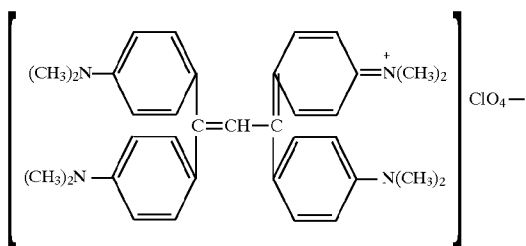
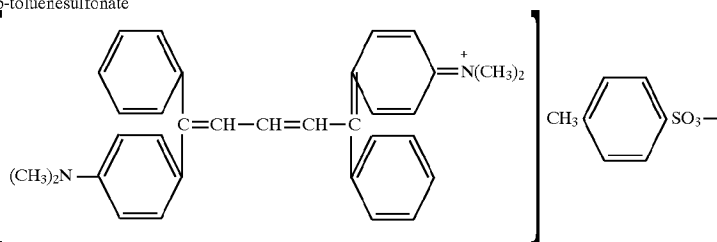
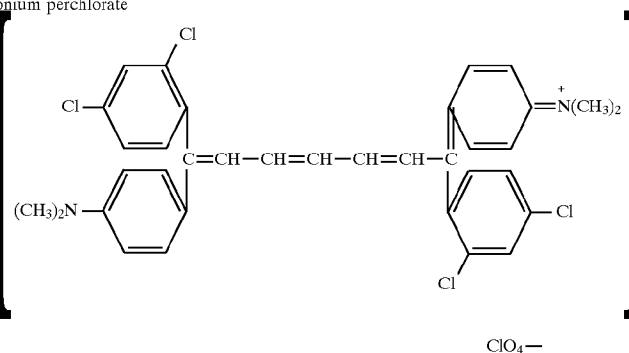
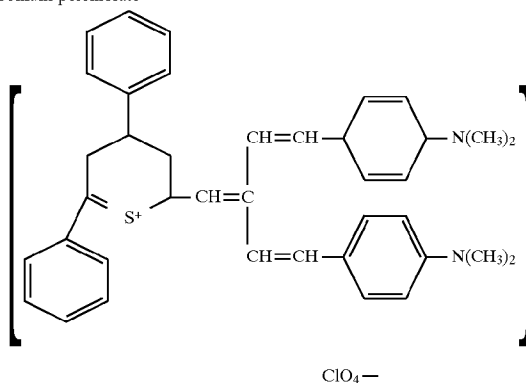
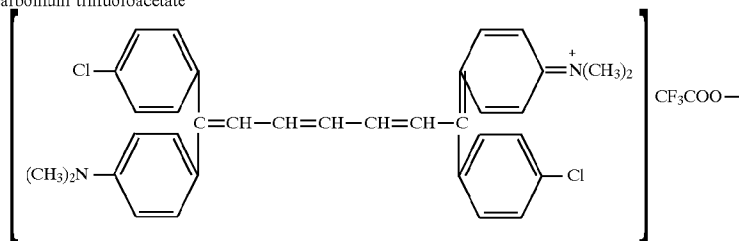
Genacryl Pink G

Sevron Brilliant - Red B

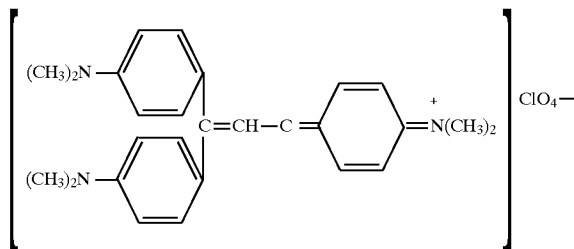
Sevron Brilliant - Red 3B

1,5-bis-[4(N,N-dimethylamino)phenyl]-1,5-bis-
(phenyl)divinyl carbonium trifluoroacetate

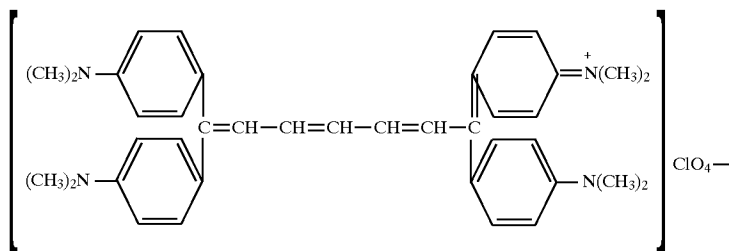


1,1,3,3-tetrakis[4(N,N-dimethylamino)phenyl]
vinyl carbonium perchlorate1,5-bis-[4(N,N-dimethylamino)phenyl]-1,5-bis-
(phenyl) divinyl carbonium p-toluenesulfonate1,7-bis[4(N,N-dimethylamino)phenyl]-1,7-bis-
(2,4-dichlorophenyl) trivinyl carbonium perchlorateDi-[4(N,N-dimethylamino)phenyl vinyl]-[2,4-di-
phenyl-6-methane thiopyran] methyl carbonium perchlorate1,7-bis-[4(N,N-dimethylamino)phenyl]-1,7-bis-
(4-chlorophenyl) trivinyl carbonium trifluoroacetate

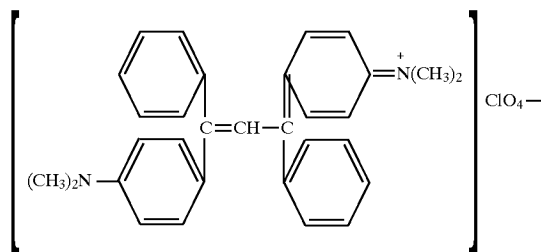
1,1,3-tris-[4-(N,N-dimethylamino)phenyl] divinyl
carbonium perchlorate



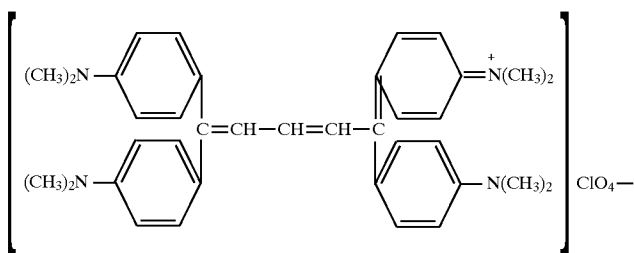
1,1,7,7-tetrakis-[4-(N,N-dimethylamino)phenyl]
trivinyl carbonium perchlorate



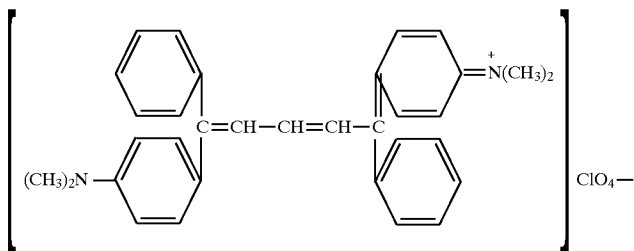
1,3-bis-[4-(N,N-dimethylamino)phenyl]-1,3-bis-
(phenyl) vinyl carbonium perchlorate



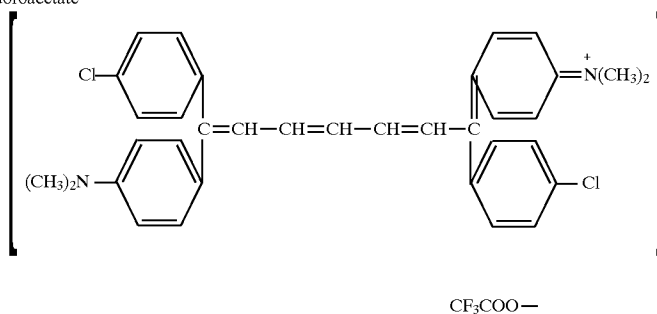
1,1,5,5-tetrakis-[4-(N,N-dimethylamino)phenyl]
divinyl carbonium perchlorate



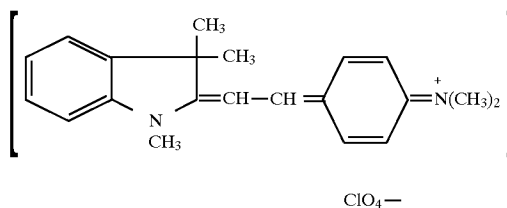
1,5-bis-[4-(N,N-dimethylamino)phenyl]-1,5-bis-
(phenyl) divinyl carbonium perchlorate



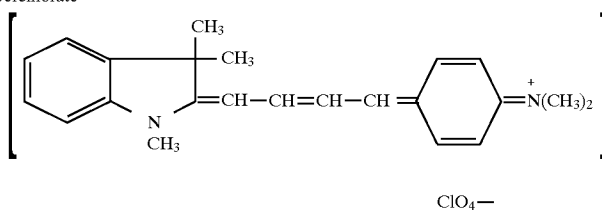
1,7-bis-[4-(N,N-dimethylamino)phenyl]-1,7-bis-(phenyl) trivinyl carbonium trifluoroacetate



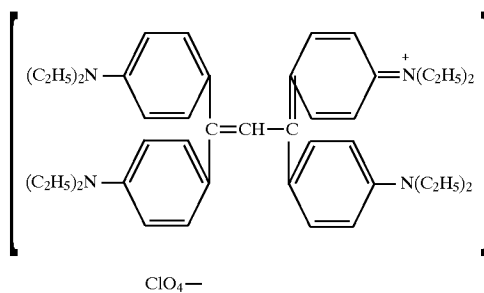
1(1,3,3-trimethyl indoline)-2-[4-(N,N-dimethylamino)phenyl] ethylene carbonium perchlorate



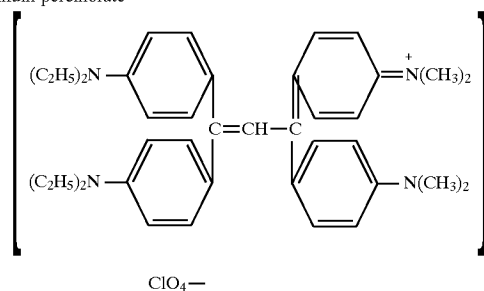
1(1,3,3-trimethyl indoline)-4-[4-(N,N-dimethylamino)phenyl] butylene carbonium perchlorate



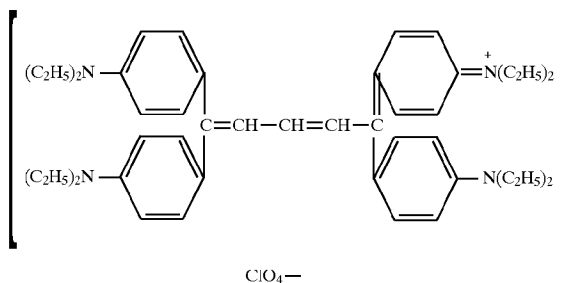
1,1,3,3-tetrakis-[4-(N,N-diethylamino)phenyl] vinyl carbonium perchlorate



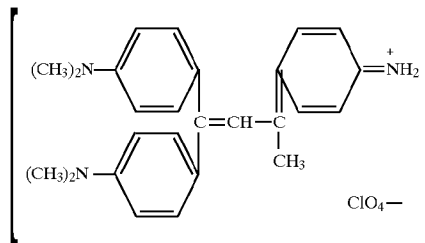
1,1-bis-[4-(N,N-diethylamino)phenyl]-3,3-bis-[4-(N,N-dimethylamino)phenyl] vinyl carbonium perchlorate



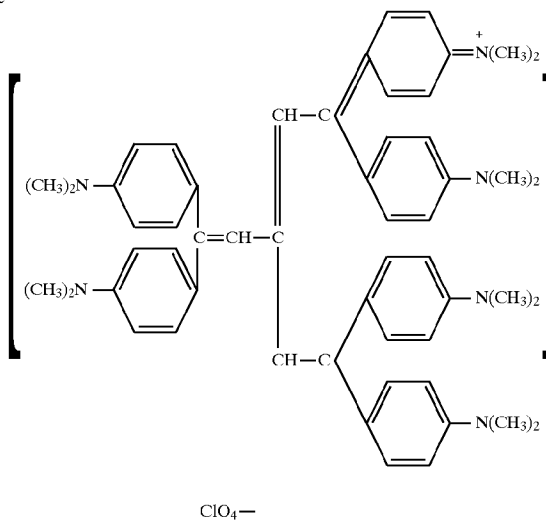
1,1,5,5-tetrakis-[4-(N,N-diethylamino)phenyl]
divinyl carbonium perchlorate



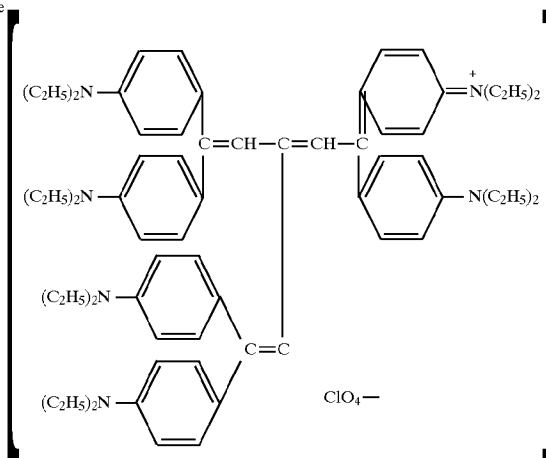
1,1-bis-[4-(N,N-dimethylamino)phenyl]-3-[4-(amino)
phenyl]-3-methylvinyl carbonium perchlorate



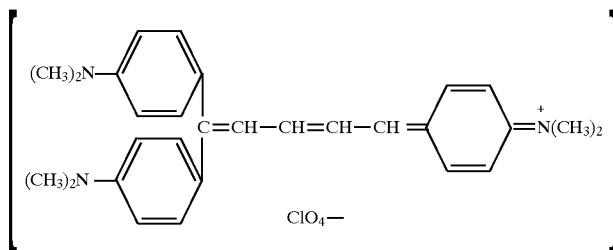
Tris-[1,1-bis-[4-(N,N-dimethylamino)phenyl]
ethylene] methyl carbonium perchlorate



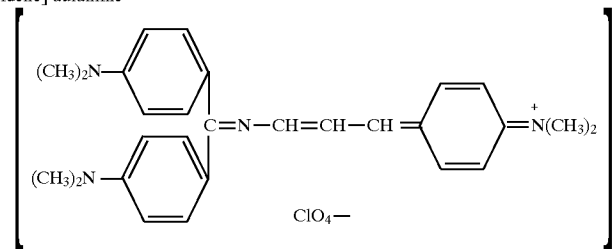
Tris-[1,1-bis-[4-(N,N-diethylamino)phenyl]
ethylene] methyl carbonium perchlorate



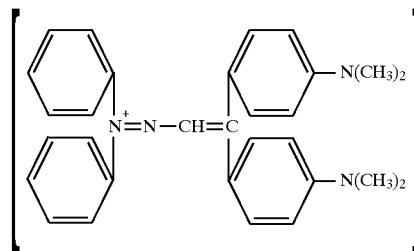
1,1,5-tris-[4-(N,N-dimethylamino)phenyl] divinyl
carbonium perchlorate



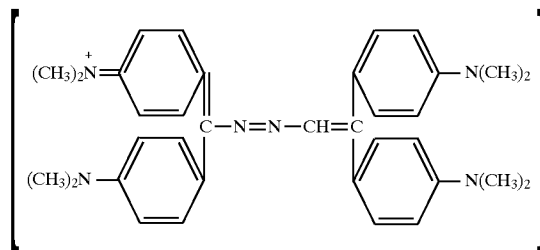
N[4-(N,N-dimethylamino) cinnamylidene] auramine



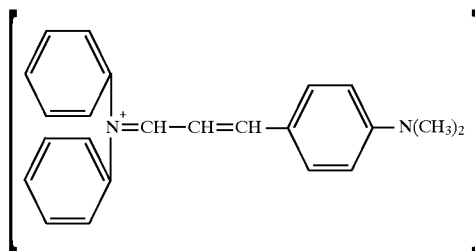
1,1-bis-[4-(N,N-dimethylamino)phenyl]-3,4-bis-
(phenyl)]-3,4-diazo butene carbonium



1,1,5,5-tetrakis-[4-(N,N-dimethylamino)phenyl]-
2,3-diazo pentene carbonium

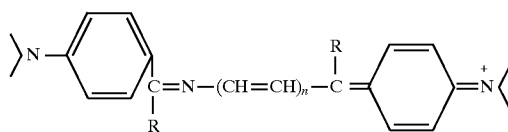


N-(N',N'-dimethylamino cinnamylidene)-N,N-diphenyl
ammonium

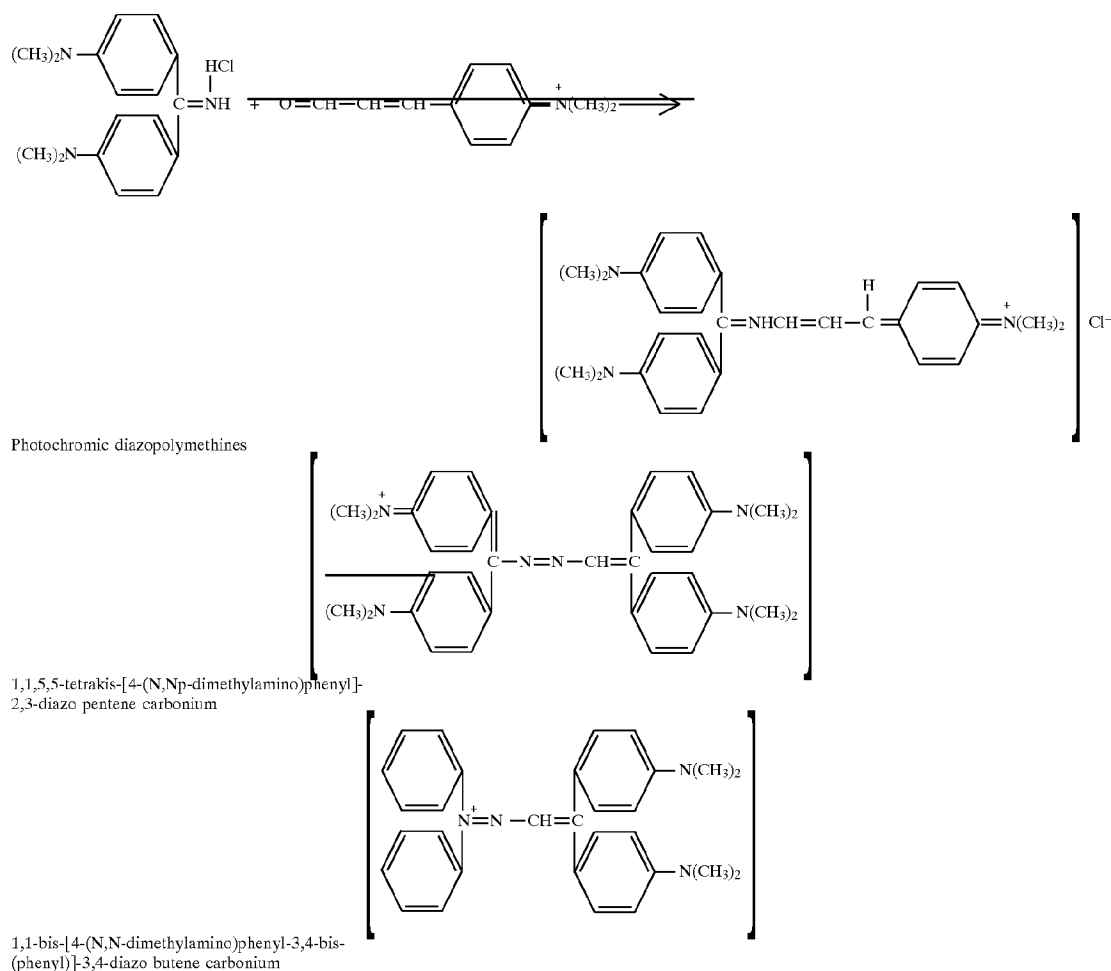


Azo Polymethines

Dyes of the general structural type



wherein each R comprises a functional group selected from the group consisting of alkyl, cycloalkyl, alkoxy, carbonyl, cyano, carbamoyl, heterocyclic rings containing C, O, N, S, sulfo, sulfamoyl, alkoxy, sulfonyl, phosphono, hydroxyl, halogen, alkoxy, alkylthiol, acyloxy, aryl, alkenyl, aliphatic, acyl, carboxyl, amino, cyanoalkoxy, diazonium, carboxyalkylcarboxamido, alkenylthio, cyanoalkoxy, carbamoylalkoxy, alkoxy carbonylamino, cyanoalkylamino, alkoxy carbonylalkylamino, sulfoalkylamino, alkylsulfamoylalkylamino, oxido, hydroxy alkyl, carboxy alkylcarboxyloxy, cyanoalkyl, carboxyalkylthio, arylamino, heteroaryl, alkoxy carbonyl, alkylcarboxyloxy, cyanoalkoxy, alkoxy carbonylalkoxy, carbamoylalkoxy, carbamoylalkyl carboxyloxy, sulfoalkoxy, nitro, alkoxyaryl, halogenaryl, amino aryl, alkylaminoaryl, tolyl, alkenylaryl, allylaryl, alkenyloxyaryl, allyloxyaryl, cyanoaryl, carbamoylaryl, carboxyaryl, alkoxy carbonylaryl, alkylcarboxyloxyaryl, sulfoaryl, alkoxy sulfoaryl, sulfamoylaryl, and nitroaryl; and



31. (Currently Amended) The method of synthesis of the compound of claim 10 wherein the

C moiety is any molecule which exhibits bleaching behavior with the B moiety and has an increased therapeutic effect or therapeutic ratio as a consequence of its delivery as part of a prodrug.

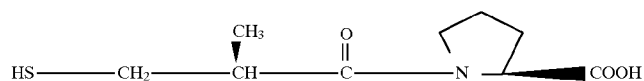
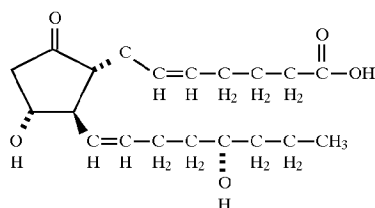
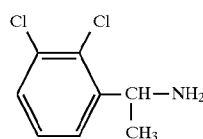
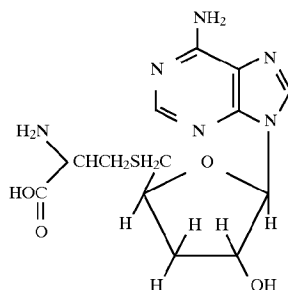
32. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 29 wherein the C moiety has a nucleophilic group that bonds to the B moiety.

33. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 32 wherein the C moiety is derivatized to have a nucleophilic group that bonds to the B moiety.

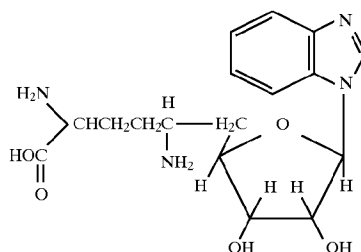
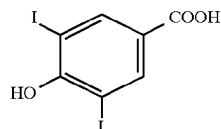
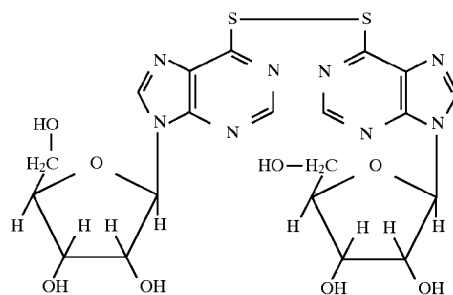
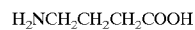
34. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 33 wherein the C moiety is derivatized by at least one of the nucleophilic groups comprising cinnamate, sulfite, phosphate, carboxylate, thiol, amide, alkoxide, or amine.

35. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 10 wherein the C moiety is at least one of the group of

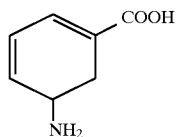
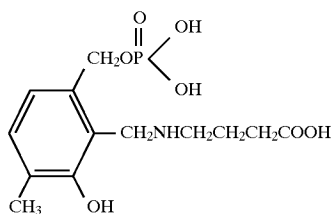
Captopril

Prostaglandin E₂2,3-dichloro- α -methyl-
benzylamine3'-deoxy-S-adenosyl-L-
homocysteine

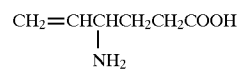
Sinefungin

3,5-diiodo-4-hydroxy-
benzoic acid6,6'-dithiebis (9-
B-D-ribofuranosylpurine) γ -aminobutyric acid

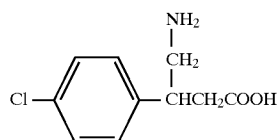
Gabaculine

N-(5'-phosphopyridoxy)-
4-aminobutyric acid

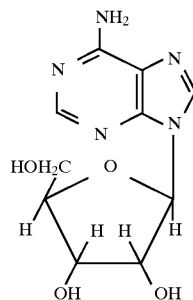
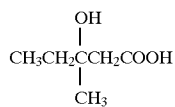
4-amino-hex-5-enoic acid



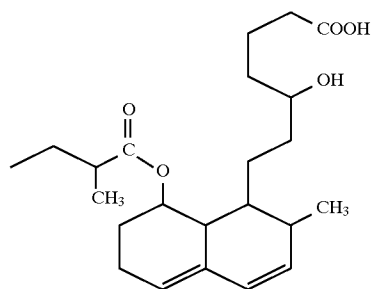
Baclofen



Adenosine

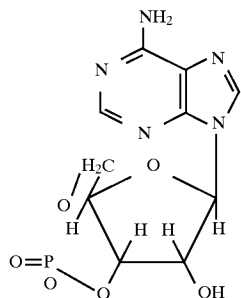
3-hydroxy-3-methyl-
glutarate

Campactin

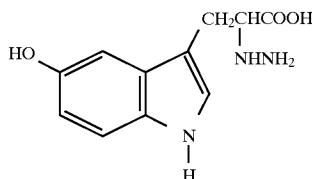


Nc1ncnc2n(cnc12)[C@H]3O[C@@H](COP(=O)([O-])OC(C)C(O)CNC(=O)CCN(CCSCC(=O)C#N)C(=O)O)[C@H](O)[C@@H](CO)[C@H]3ONCCc1ccc(O)c(I)c1CC(N)C(=O)Cc1ccc(I)cc1O[Na+].[O-]C(=O)C1=CC(=C2C(=C1)C(=O)C=C2OC3=CC=CC=C3OCC(O)CCOC4=CC(=C5C(=C4)C(=O)C=C5OC(=O)[O-])[O-])[Na+]

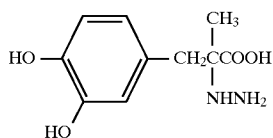
Adenosine
3',5'-cyclic monophosphate



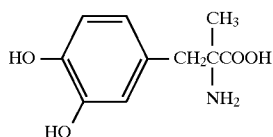
D,L-B-(5-hydroxy-3-indolyl)- α -hydrazinopropionic acid



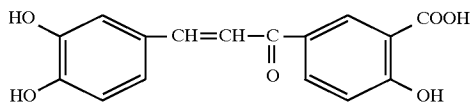
D,L- α -hydrazino- α -methyl dopa



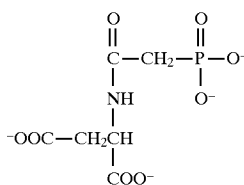
α -methyl dopa



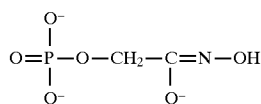
5-(3,4-dihydroxycinnamoyl)salicylic acid



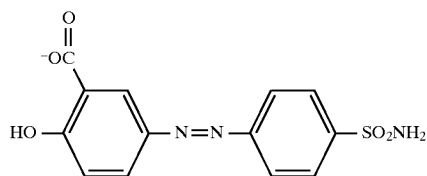
N-(phosphonacetyl)-L-aspartate



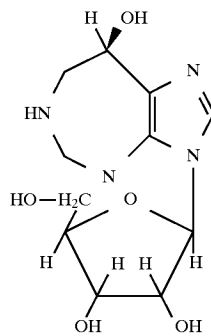
P-glycolohydroxamate



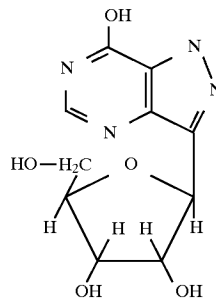
5-(p-sulfamylphenyl)azosalicylic acid



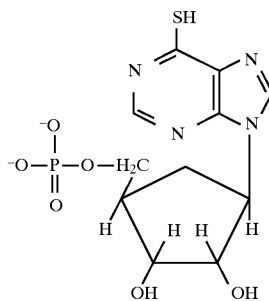
Coformycin



Formycin B



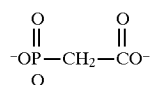
Thioinosinate



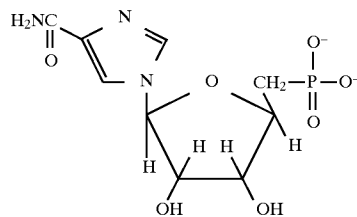
Phosphonoformate



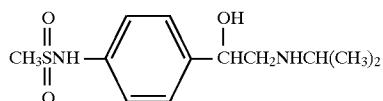
Phosphonoacetate



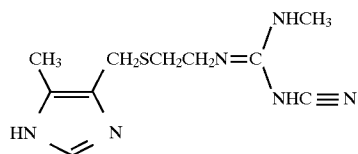
Ridavirin



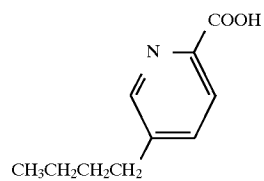
Sotalol



Cimetidine



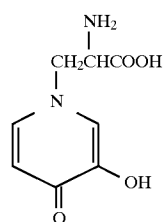
Fuscaric acid



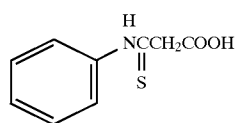
2-mercaptoethylamine



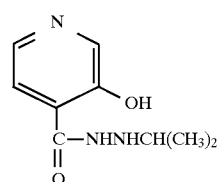
Mimosine



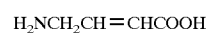
U-7130



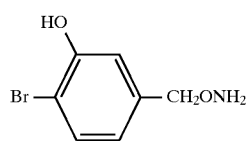
Iproniazid



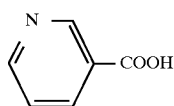
Trans-4-aminocrotonic acid



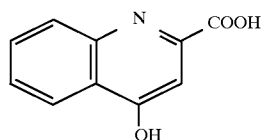
NSD 1055



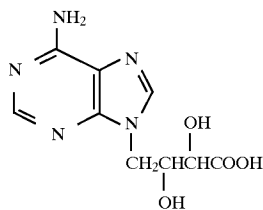
Nicotinic acid



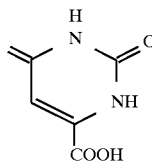
Kynurenic acid



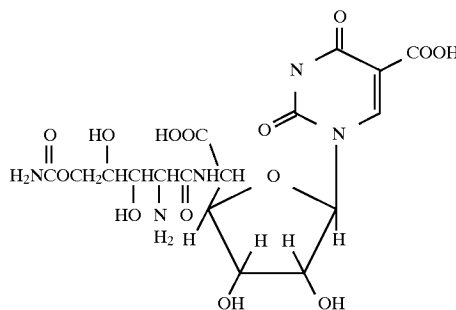
Lentysine



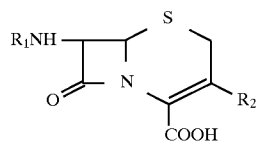
Orotic acid



Polyoxin D

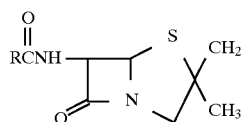


Cephalosporin



, and

Penicillin



36. (Canceled)

37. (Currently Amended) The method of synthesis of the compound of claim 1 wherein the C moiety comprises at least one of the group of herbicides, fungicides, miticides, nematocides, fumigants, growth regulators, repellants, defoliants, rodenticides, molluscicides, algicides, desiccants, antehelminthics, and bactericides.

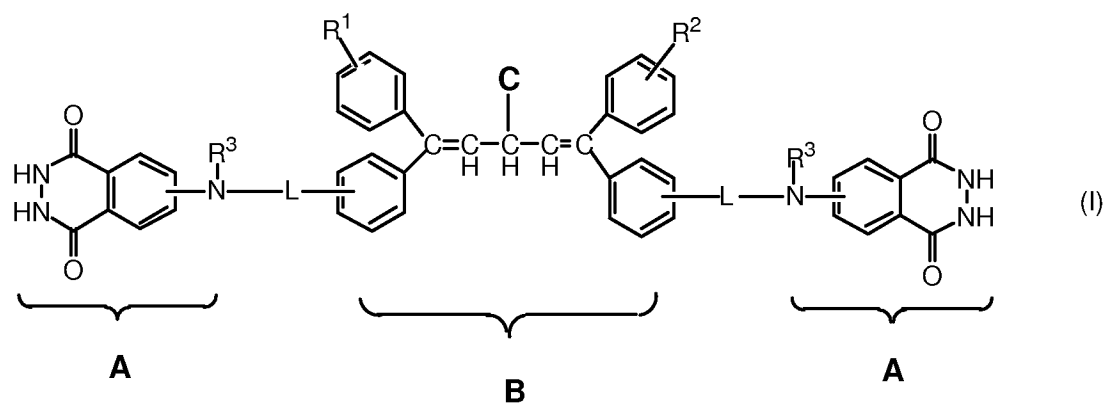
38. (Currently Amended) The method of synthesis of the compound of claim 37 wherein the C moiety is a pesticide.

39-70. (Cancelled)

71. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein one or more of the moieties can be modified to further candidate components by addition of functional groups.

72. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 71 wherein the groups comprise at least one of alkyl, cycloalkyl, alkoxy carbonyl, cyano, carbamoyl, heterocyclic rings containing C, O, N, S, sulfo, sulfamoyl, alkoxy sulfonyl, phosphono, hydroxyl, halogen, alkoxy, alkylthiol, acyloxy, aryl, alkenyl, aliphatic, acyl, carboxyl, amino, cyanoalkoxy, diazonium, carboxyalkylcarboxamido, alkenylthio, cyanoalkoxy carbonyl, carbamoylalkoxy carbonyl, alkoxy carbonylamino, cyanoalkylamino, alkoxy carbonylalkylamino, sulfoalkylamino, alkylsulfamoylalkylamino, oxido, hydroxy alkyl, carboxy alkylcarbonyloxy, cyanoalkyl, carboxyalkylthio, arylamino, heteroaryl amino, alkoxy carbonyl, alkylcarbonyloxy, cyanoalkoxy, alkoxy carbonylalkoxy, carbamoylalkoxy, carbamoylalkyl carbonyloxy, sulfoalkoxy, nitro, alkoxyaryl, halogenaryl, amino aryl, alkylaminoaryl, tolyl, alkenylaryl, allylaryl, alkenyloxyaryl, allyloxyaryl, cyanoaryl, carbamoylaryl, carboxyaryl, alkoxy carbonylaryl, alkylcarbonyoxyaryl, sulfoaryl, alkoxy sulfoaryl, sulfamoylaryl, and nitroaryl.

73. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein the compound has the structure of general formula



where R^1 , R^2 , and R^3 ~~[[are]]~~ are functional groups independently selected from the group consisting of alkyl, cycloalkyl, alkoxy carbonyl, cyano, carbamoyl, heterocyclic rings containing

C, O, N, S, sulfo, sulfamoyl, alkoxy sulfonyl, phosphono, hydroxyl, halogen, alkoxy, alkylthiol, acyloxy, aryl, alkenyl, aliphatic, acyl, carboxyl, amino, cyanoalkoxy, diazonium, carboxyalkylcarboxamido, alkenylthio, cyanoalkoxycarbonyl, carbamoylalkoxycarbonyl, alkoxy carbonylamino, cyanoalkylamino, alkoxy carbonylalkylamino, sulfoalkylamino, alkylsulfamoylalkylamino, oxido, hydroxy alkyl, carboxy alkylcarbonyloxy, cyanoalkyl, carboxyalkylthio, arylamino, heteroaryl, alkoxy carbonyl, alkylcarbonyloxy, cyanoalkoxy, alkoxy carbonylalkoxy, carbamoylalkoxy, carbamoylalkyl carbonyloxy, sulfoalkoxy, nitro, alkoxyaryl, halogenaryl, amino aryl, alkylaminoaryl, tolyl, alkenylaryl, allylaryl, alkenyloxyaryl, allyloxyaryl, cyanoaryl, carbamoylaryl, carboxyaryl, alkoxy carbonylaryl, alkylcarbonyoxyaryl, sulfoaryl, alkoxy sulfoaryl, sulfamoylaryl, and nitroaryl; and L is a linker.

74. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 73 wherein the functionality **A** is at least one of ~~aminophthalhydrazide derivatives~~, sulfonyloxamides and active oxalates;

~~the functionality **B** is at least one of 1,1,5,5 tetrakisarylpentadiene and 1,1,5-trisarylpentadiene derivatives,~~

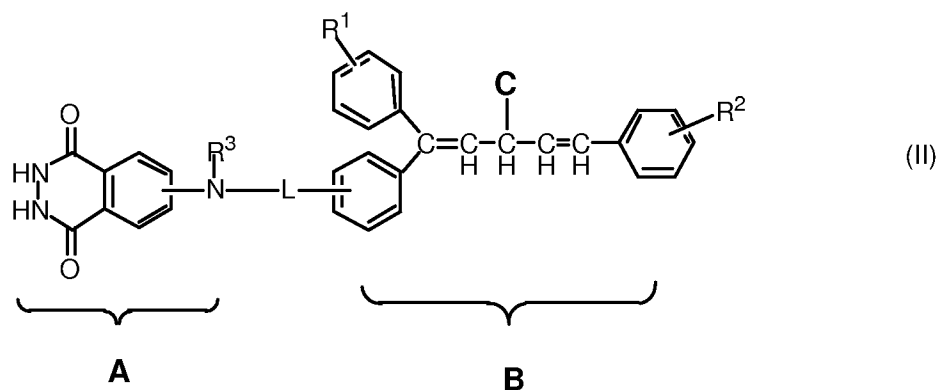
~~the functionality **C** is a drug molecule such as Foscarinate, or ddc;, and~~

~~R is a functional group, and~~

~~L is a linker such as an aliphatic chain between A and B.~~

75. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 74 wherein the L functionality is between one and 20 carbon atoms.

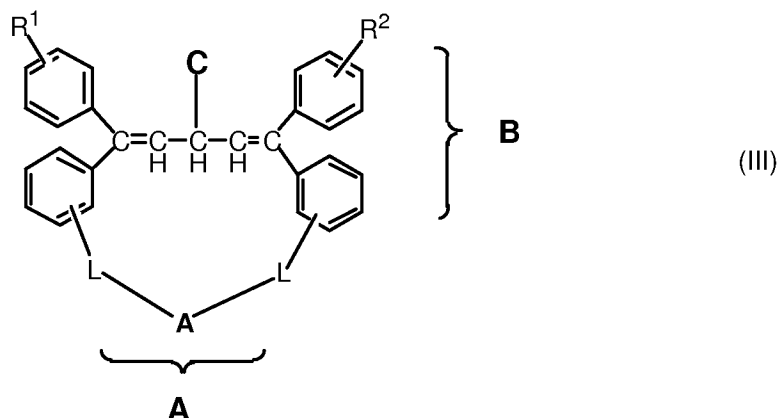
76. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein ~~B is a 1,1,5 trisarylpentadiene derivative and~~ the compound has the formula



where R^1 , R^2 , and R^3 are functional groups independently selected from the group consisting of

alkyl, cycloalkyl, alkoxycarbonyl, cyano, carbamoyl, heterocyclic rings containing C, O, N, S, sulfo, sulfamoyl, alkoxysulfonyl, phosphono, hydroxyl, halogen, alkoxy, alkylthiol, acyloxy, aryl, alkenyl, aliphatic, acyl, carboxyl, amino, cyanoalkoxy, diazonium, carboxyalkylcarboxamido, alkenylthio, cyanoalkoxycarbonyl, carbamoylalkoxycarbonyl, alkoxy carbonylamino, cyanoalkylamino, alkoxycarbonylalkylamino, sulfoalkylamino, alkylsulfamoylalkylamino, oxido, hydroxy alkyl, carboxy alkylcarbonyloxy, cyanoalkyl, carboxyalkylthio, arylamino, heteroaryl, alkoxy, carbonylamino, alkylcarbonyloxy, cyanoalkoxy, alkoxycarbonylalkoxy, carbamoylalkoxy, carbamoylalkyl carbonyloxy, sulfoalkoxy, nitro, alkoxyaryl, halogenaryl, amino aryl, alkylaminoaryl, tolyl, alkenylaryl, allylaryl, alkenyloxyaryl, allyloxyaryl, cyanoaryl, carbamoylaryl, carboxyaryl, alkoxycarbonylaryl, alkylcarbonyoxyaryl, sulfoaryl, alkoxysulfoaryl, sulfamoylaryl, and nitroaryl; and L is a linker.

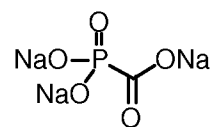
77. (Currently Amended) The method of synthesis of the compound of claim 1 wherein A is a sulfonyloxamide or active oxalate and the compound has the formula



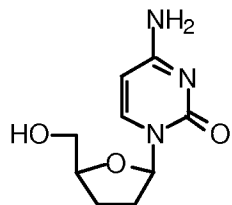
where R^1 , R^2 , and R^3 are functional groups independently selected from the group consisting of alkyl, cycloalkyl, alkoxycarbonyl, cyano, carbamoyl, heterocyclic rings containing C, O, N, S, sulfo, sulfamoyl, alkoxysulfonyl, phosphono, hydroxyl, halogen, alkoxy, alkylthiol, acyloxy, aryl, alkenyl, aliphatic, acyl, carboxyl, amino, cyanoalkoxy, diazonium, carboxyalkylcarboxamido, alkenylthio, cyanoalkoxycarbonyl, carbamoylalkoxycarbonyl, alkoxy carbonylamino, cyanoalkylamino, alkoxycarbonylalkylamino, sulfoalkylamino, alkylsulfamoylalkylamino, oxido, hydroxy alkyl, carboxy alkylcarbonyloxy, cyanoalkyl, carboxyalkylthio, arylamino, heteroaryl, alkoxy, carbonylamino, alkylcarbonyloxy, cyanoalkoxy, alkoxycarbonylalkoxy, carbamoylalkoxy, carbamoylalkyl carbonyloxy, sulfoalkoxy, nitro, alkoxyaryl, halogenaryl, amino aryl, alkylaminoaryl, tolyl, alkenylaryl, allylaryl, alkenyloxyaryl, allyloxyaryl, cyanoaryl, carbamoylaryl, carboxyaryl, alkoxycarbonylaryl, alkylcarbonyoxyaryl, sulfoaryl, alkoxysulfoaryl, sulfamoylaryl, and nitroaryl; and L is a linker.

78. (Cancelled)

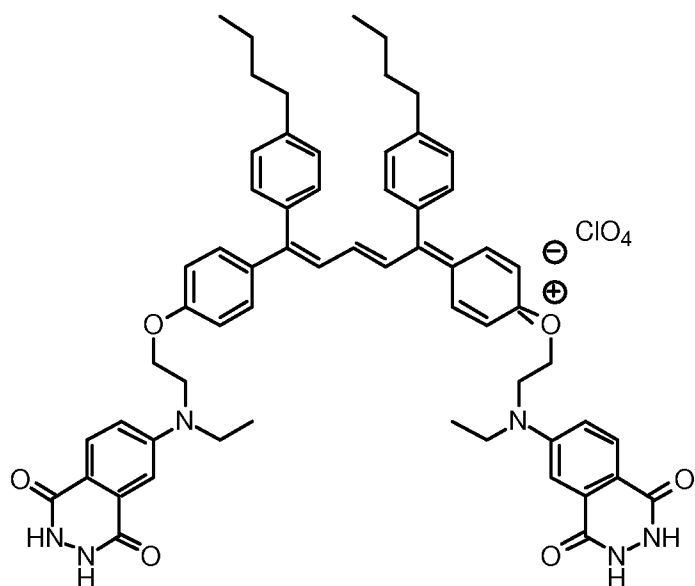
79. (Currently Amended) The method of synthesis of the compound of claim ~~[[78]]~~1 wherein C comprises the formula of at least one of



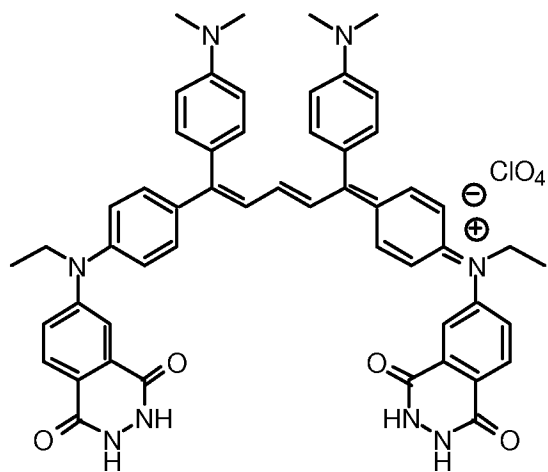
Foscarnet and



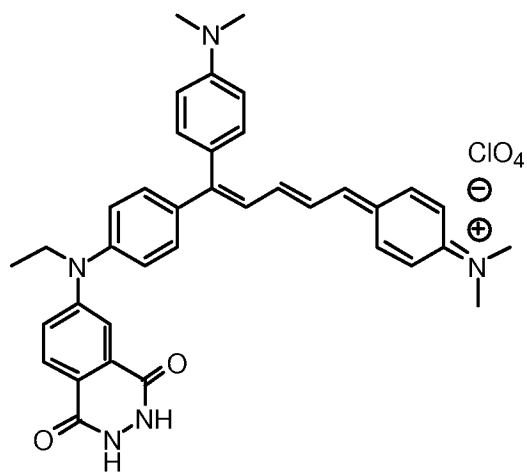
ddc, and A-B comprises the formula of at least one of



YY99811-1



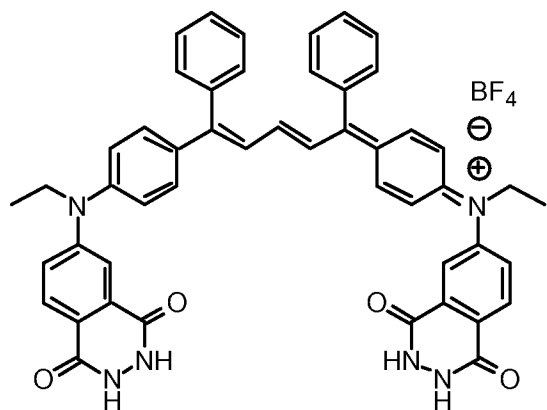
6a



GZW2-33-1

$$\text{C}_{37}\text{H}_{38}\text{N}_5\text{O}_2 \cdot \text{ClO}_4$$

M.W. 684.20



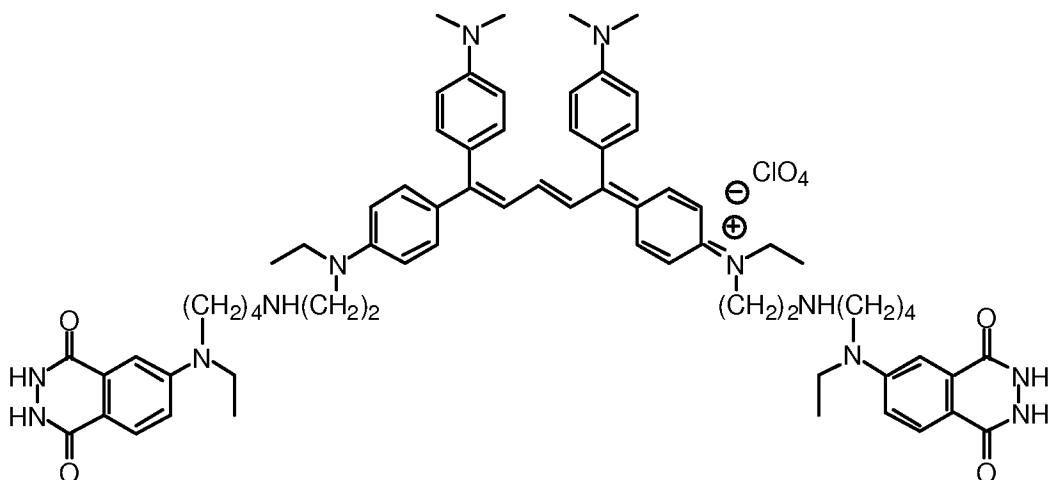
GZW1-98-2

 $C_{49}H_{41}N_6O_4 \cdot BF_4$

M.W. 864.71

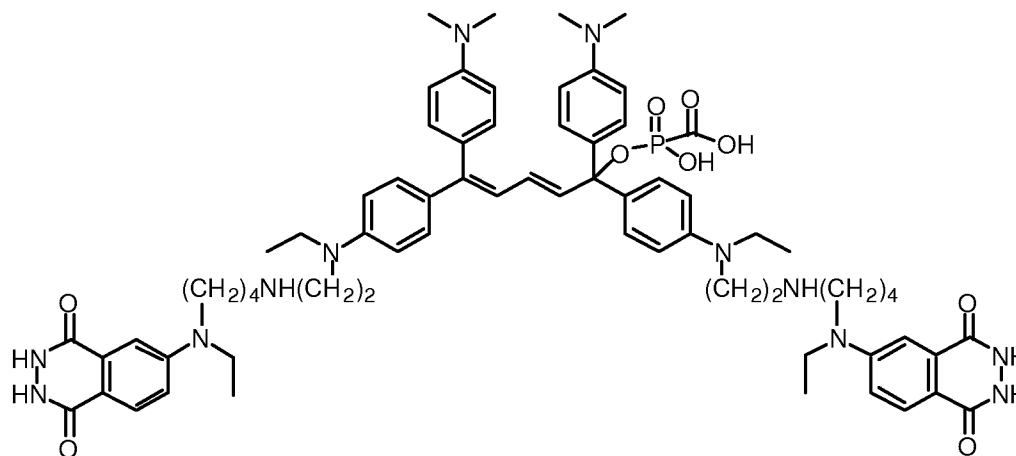
, and

MTLJ-1



80. (Currently Amended) The method of synthesis of the compound of claim [[78]]1 wherein the compound comprises the formula

MTLJ-1-Foscarnet



81. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein the hydrolyzable group that protects phthalhydrazide is at least one of acetyl and t-butyloxycarbonyl.

82. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein the aminophthalimide-substituted precursors for the dye are prepared through amination of an aryl halide such as palladium-catalyzed amination of aryl halides.

83. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein halo-substituted aryl groups of a starting B moiety or an intermediate are coupled with the aminophthalimide by methods such as the aryl amination under palladium catalysis to form the aminophthalimide-substituted precursors for the dye.

84. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein halo-substituted aryl groups of a starting phthalimide or an intermediate are coupled with the amino-substituted dye by methods such as the aryl amination under palladium catalysis to form the aminophthalimide-substituted precursors for the dye.

85. (Currently Amended) The method ~~of synthesis of the compound~~ of claims 84 wherein ~~amino-substituted aryl groups are obtained by the amination of the halo-substituted phthalimide~~ is exposed to an compounds with an imine or a such as benzophenoneimine, thereby generating an amino substituted aryl group.

86. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein the aminophthalimide-attached dye is formed by the condensation of two aminophthalimide-attached ethylene molecules by reaction with triethyl orthoformate and a strong acid such as perchloric acid in acetic anhydride or acetic acid.

87. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein during the step of converting the phthalimide moiety to the aminophthalhydrazide to obtain A-B, the B moiety is protected from reaction with hydrazine by reacting with base such as sodium hydroxide, sodium methoxide and amines.

88. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 87 wherein the phthalimide-B conjugate with a protected B moiety is refluxed with hydrazine in a suitable solvent such as an alcoholic solvent in inert atmosphere and then treated with acid such as perchloric acid, tetrafluoroboric acid to regenerate a corresponding unaltered B moiety of the A-B conjugate.

89. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 88 wherein A-B is reacted with one nucleophilic species of C to form A-B-C.

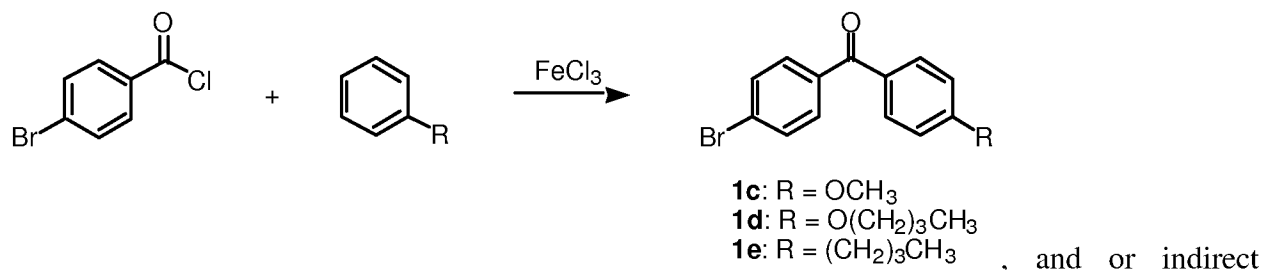
90. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein A-B is formed by starting with B comprising halo-substituted dyes, such as 1,5-bis(p-bromophenyl)-1,5-bis(p-dimethylaminophenyl)-pentadienium perchlorate.

91. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 90 wherein cationic dyes are protected by reacting with base such as alkoxide and then coupled with the aminophthalimide by amination of aryl halide such as the palladium-catalyzed amination of aryl halide to obtain the alkoxide-protecting aminophthalimide-substituted dyes.

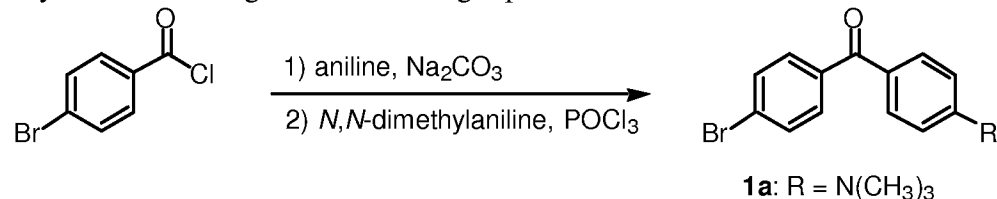
92. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 91 wherein the aminophthalimide-B conjugate with a protected B moiety is refluxed with hydrazine in a suitable solvent such as an alcoholic solvent to convert the amino-phthalimide moiety to the aminophthalhydrazide moiety and then treated with acid to generate A-B.

93. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 wherein the B comprises a tetraarylpolymethine, the aminophthalhydrazide precursor is an aminophthalic acid diester and the conjugate to form A-B is amino-phthalimideluminol-tetraaryl-polymethine.

94. (Currently Amended) The method of ~~synthesis of the compound~~ of claim 1 wherein halo-substituted diarylketone are formed by at least one of direct acylation of arene with halo-substituted benzoyl halide under ferric chloride catalysis according to the following representative scheme



acylation according to the following representative scheme



95. (Currently Amended) The method of ~~synthesis of the compound~~ of claim 1 wherein a halo-substituted diarylketone is converted to the corresponding halo-substituted diarylketene such as halo-substituted 1,1-diarylethene.

96. (Currently Amended) The method of ~~synthesis of the compound~~ of claim 95 wherein the halo-substituted diarylketene is coupled with a precursor of amino-phthalhydrazide such as aminophthalimide, aminophthalic acid diester, by aryl amination such as the palladium-catalyzed amination of aryl halides to form the aminophthalimide-substituted 1,1-diarylethene.

97. (Currently Amended) The method of ~~synthesis of the compound~~ of claim 96 wherein the ethene is condensed with an orthoester such as triethylorthoformate in a nonaqueous solvent such as acetic anhydride, containing an acid catalyst such as perchloric acid, tetrafluoroboric acid, to form the aminophthalimide-substituted tetraarylpolymethine dye.

98. (Currently Amended) The method of ~~synthesis of the compound~~ of claim 97 wherein the aminophthalimide moiety is converted to the aminophthalhydrazide to obtain A-B.

99. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 98 wherein the B moiety is a cationic dye that is first protected by reacting with an anion such as hydroxide, methoxide and amine and the phthalimide-B conjugate with a protected B moiety is refluxed with hydrazine in a suitable solvent such as an alcoholic solvent in inert atmosphere and then treated with acid such as perchloric acid, tetrafluoroboric acid to regenerate a corresponding unaltered B moiety of the A-B conjugate.

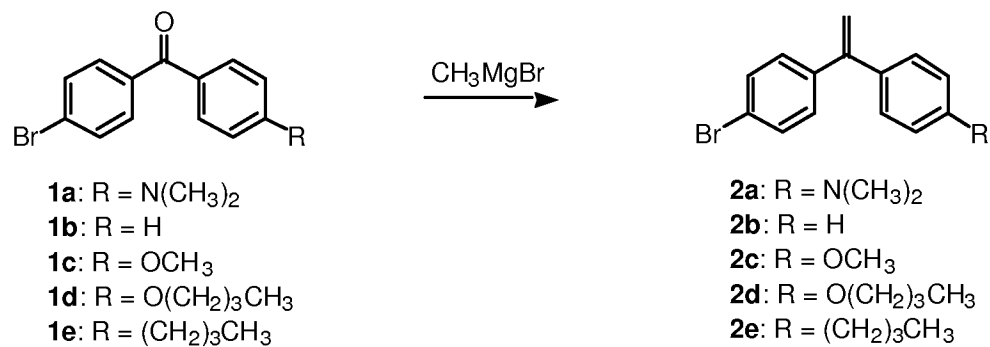
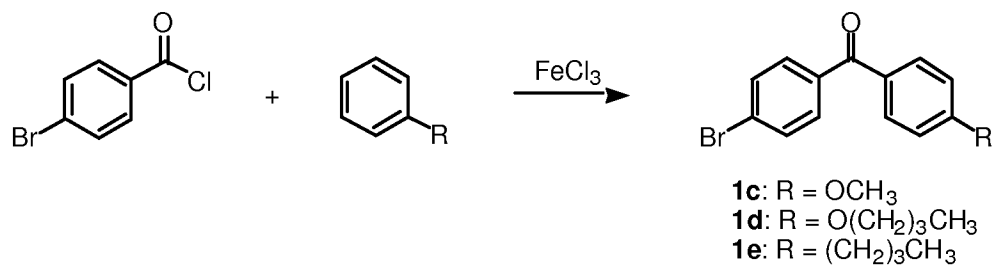
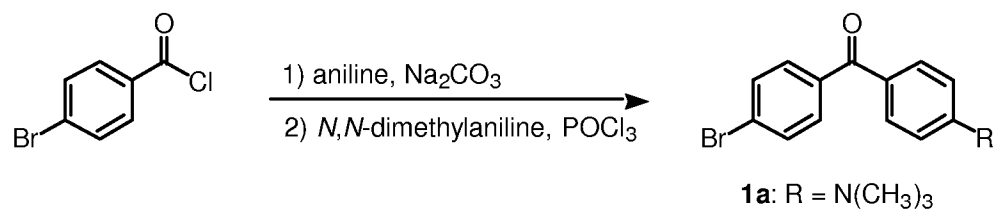
100. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 99 wherein A-B is reacted with one nucleophilic species of a C such as a drug 2',3'-dideoxycytidine, Foscarnet, acycloguanosine to form A-B-C comprising a prodrug.

101. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 95 wherein two halo-substituted diarylketene precursor compounds are condensed with an orthoester such as triethylorthoformate in a nonaqueous solvent such as acetic anhydride containing acid catalyst such as perchloric acid, tetrafluoroboric acid to form the halo-substituted tetraarylpolymethine dyes such as 1,5-bis(p-bromophenyl)-1,5-bis(p-dimethylaminophenyl)-pentadienium perchlorate.

102. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 101 wherein the B moiety is a cationic dye that is protected by reacting with an anion such as alkoxide and then coupled with the aminophthalimide by amination of aryl halide such as the palladium-catalyzed amination of aryl halide to obtain the alkoxide-protected aminophthalimide-substituted tetraarylpolymethine dye.

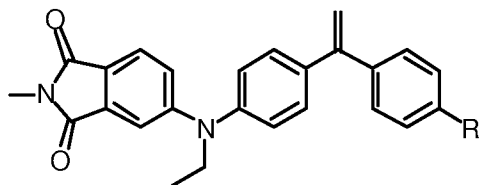
103. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 103 wherein the alkoxide-protected aminophthalimide-substituted tetraarylpolymethine dye is refluxed with hydrazine in a suitable solvent such as an alcoholic solvent to convert the amino-phthalimide moiety to the aminophthalhydrazide moiety and then treated with acid to generate A-B comprising a luminol-tetraarylpolymethine compound.

104. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 1 comprising the general steps given by following representative formula

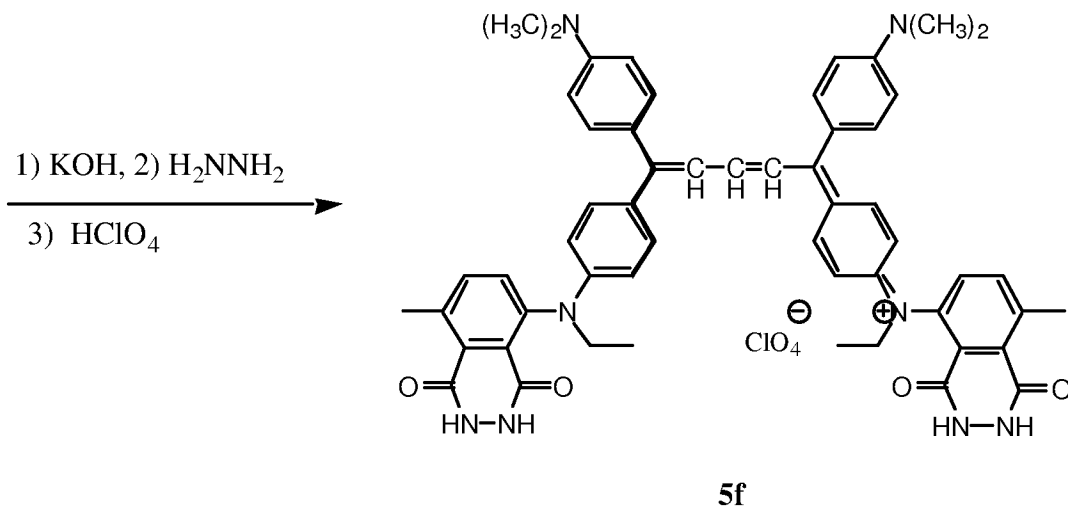
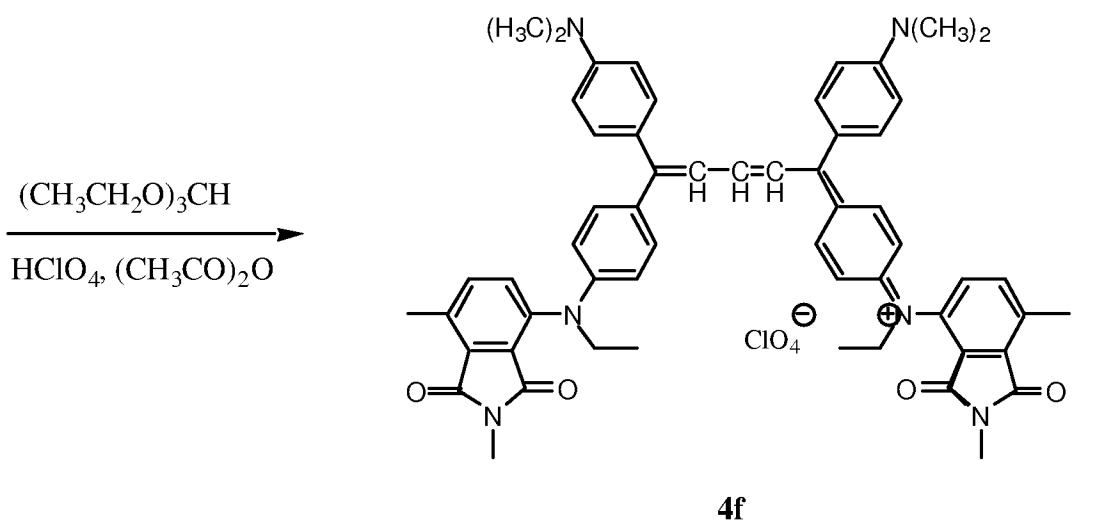
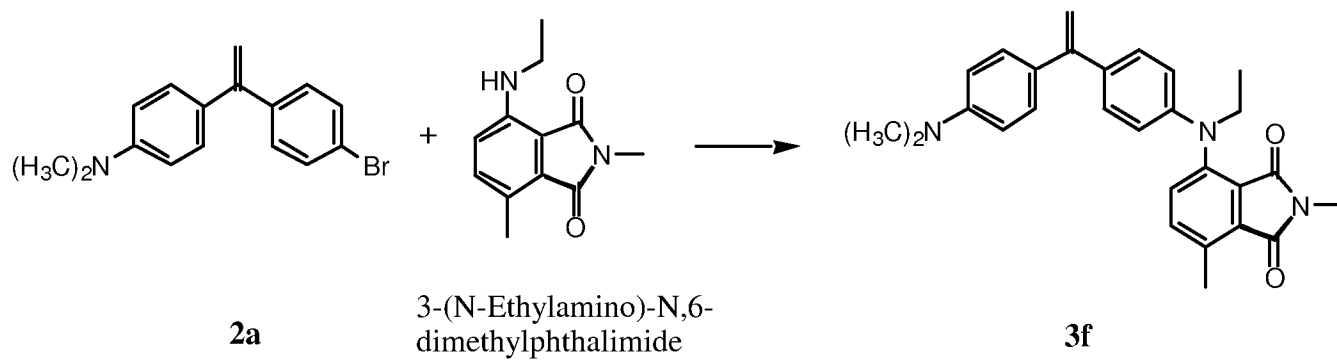


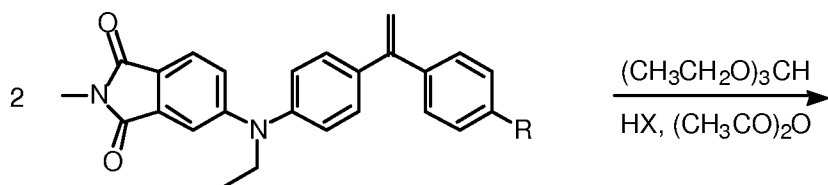
4-(*N*-ethylamino)-*N*-methylphthalimide

$\text{Pd}(\text{OAc})_2$, $\text{P}(t\text{-Bu})_3$,
 $t\text{-BuONa}$



3a: $\text{R} = \text{N}(\text{CH}_3)_2$
3b: $\text{R} = \text{H}$
3c: $\text{R} = \text{OCH}_3$
3d: $\text{R} = \text{O}(\text{CH}_2)_3\text{CH}_3$
3e: $\text{R} = (\text{CH}_2)_3\text{CH}_3$





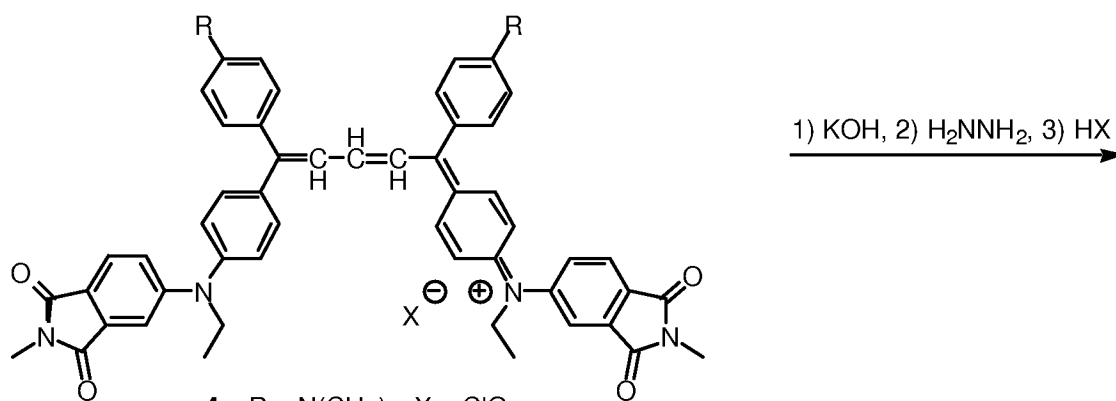
3a: R = N(CH₃)₂

3b: R = H

3c: R = OCH₃

3d: R = O(CH₂)₃CH₃

3e: R = (CH₂)₃CH₃



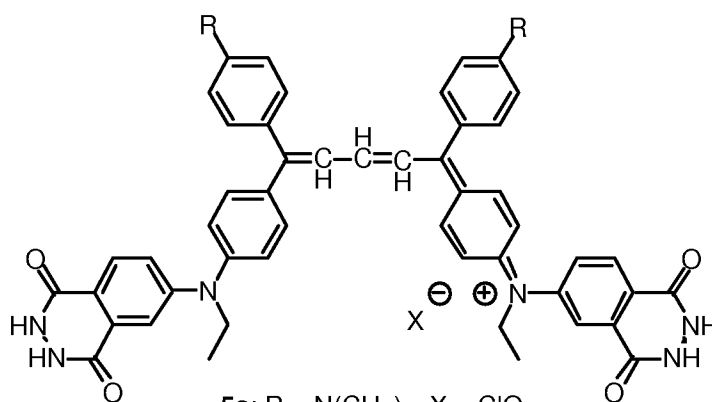
4a: R = N(CH₃)₂, X = ClO₄

4b: R = H, X = BF₄

4c: R = OCH₃, X = BF₄

4d: R = O(CH₂)₃CH₃, X = BF₄

4e: R = (CH₂)₃CH₃, X = BF₄



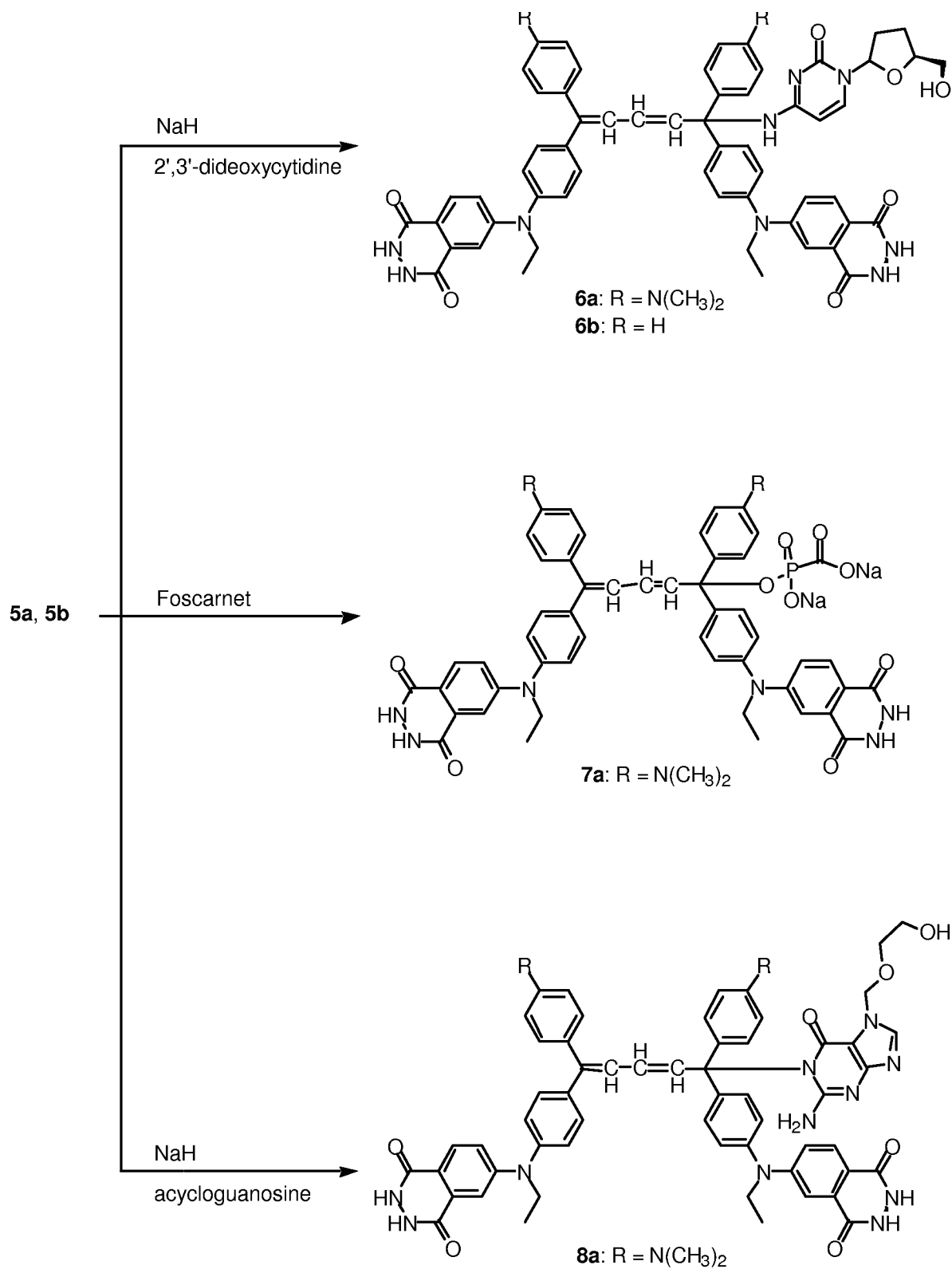
5a: R = N(CH₃)₂, X = ClO₄

5b: R = H, X = BF₄

5c: R = OCH₃, X = BF₄

5d: R = O(CH₂)₃CH₃, X = BF₄

5e: R = (CH₂)₃CH₃, X = BF₄



105. (Currently Amended) The method of synthesis of the compound of claim 1 wherein the

A functionality comprises a phthalhydrazide ~~such as a luminol derivative~~ and the B functionality comprises a photochromic dye wherein A is attached to aryl groups of B comprising the steps of

- forming a diaryl ketone,
- forming a diaryl ketene from the diaryl ketone,
- forming a protected aminophthalhydrazide such as aminophthalimide or aminophthalic acid diester,
- adding a hydrocarbon linker to the protected aminophthalhydrazide, and
- attaching the protected aminophthalhydrazide through the molecular linker to the aryl groups of diarylketene to form the precursor aminophthalimide-linked diarylketene, and reacting according to at least one of

- (a) forming the A functionality from the precursor, and condensing two molecules of B precursor linked to A to form A-B, and
- (b) condensing two precursor aminophthalimide-linked diarylketene molecules to form A precursor linked to B, and

forming the A functionality from the A precursor to form A-B.

106. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 105 wherein the diaryl ketone is formed by a classical Friedel-Crafts acylation between a benzoyl halide and aryl compound with a hydrocarbon linker having a leaving group.

107. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 106 wherein the aryl compound with a hydrocarbon linker having a leaving group comprises at least one of a halogenated-alkyl-aryl ether and a halogenated-aklyl-aryl amine wherein the halogen is the leaving group.

108. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 107 wherein the halogenated-alkyl-aryl ether comprises 2-bromoethoxybenzene to give an aryl ketone such as 4-(2-bromoethoxy)benzophenone.

109. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 107 wherein the halogenated-aklyl-aryl amine comprises 2-bromoethyl aminobenzene to give an aryl ketone such as 4-(2-bromoethyl amino)benzophenone.

110. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 105 wherein the diaryl ketone is converted to the corresponding diarylketene by reacting with a methylating reagent such as a methyl Grignard reagent, methyl lithium reagent, lithium dimethylcopper

reagent and then dehydration with acid.

111. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 110 wherein the diaryl ketone is converted to the corresponding diarylketene by reacting with methylmagnesium bromide and then dehydration with acid.

112. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 105 wherein the diaryl ketone is converted to the corresponding diarylketene by a Wittig reaction.

113. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 105 wherein a linker is attached to the protected aminophthalhydrazide by a reaction of a nucleophilic group of the linker or protected aminophthalhydrazide with a leaving group of the linker or protected aminophthalhydrazide.

114. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 105 wherein a linker is attached to the protected aminophthalhydrazide by reaction to form a bond between at least one of a nitrogen, oxygen, or carbon atom of the linker and at least one of a nitrogen, oxygen, or carbon atom of group of the protected aminophthalhydrazide by an addition or a substitution reaction of a leaving group.

115. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 114 wherein a linker is attached to the protected aminophthalhydrazide by a substitution reaction of at least one of a halogen, tosylate group, ester group with a nitrogen, oxygen, or carbon atom.

116. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 105 wherein attaching the protected aminophthalhydrazide through the molecular linker to one of the aryl groups of diarylketene to form the precursor aminophthalimide-linked diarylketene is by a reaction of a nucleophilic group of the linker or aryl group of diarylketene with a leaving group of the linker or aryl group of diarylketene.

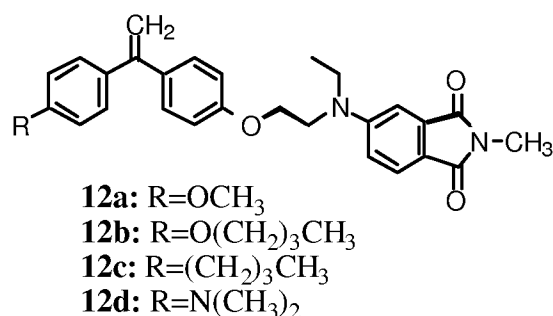
117. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 116 wherein a linker is attached to the aryl group of diarylketene by reaction to form a bond between at least one of a nitrogen, oxygen, or carbon atom of the linker and at least one of a nitrogen, oxygen, or carbon atom of group of the protected aminophthalhydrazide by an addition or a substitution reaction of a leaving group.

118. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 117 wherein a linker is attached to the aryl group of diarylketene by a substitution reaction of at least one of a halogen, tosylate group, ester group with a nitrogen, oxygen, or carbon atom.

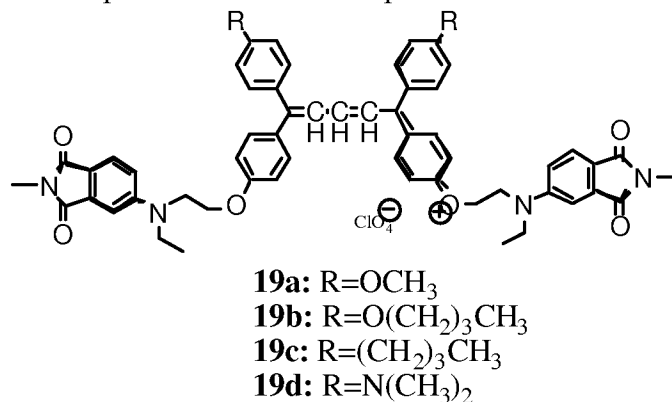
119. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 105 wherein the precursor aminophthalimide-linked diarylketene is further reacted by condensation of two aminophthalimide-linked diarylketenes with an orthoester to form B linked to the A precursor.

120. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 119 wherein condensing reagent is triethylorthoformate.

121. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 119 wherein the precursor aminophthalimide-linked diarylketene comprises at least one of the formula



and the precursor of A-B comprises at least one of the formula



122. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 119 wherein the phthalimide moiety of the A precursor is converted to the phthalhydrazide A functionality by treating with hydrazine, forming A-B.

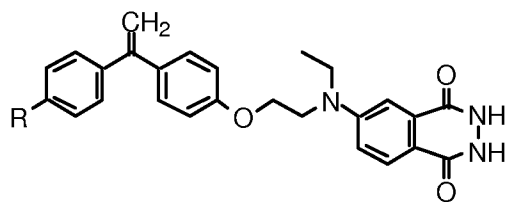
123. (Currently Amended) The method ~~of synthesis of the compound~~ of claim[[s]] 122 wherein the B functionality is protected by reacting with an anion such as hydroxide, methoxide and amine, the A-B precursor is refluxed with hydrazine in a suitable solvent such as an alcoholic solvent in inert atmosphere and then treated with acid such as perchloric acid, tetrafluoroboric acid to form A-B.

124. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 105 wherein the phthalimide moiety of the A precursor of the precursor aminophthalimide-linked diarylketene is converted to the phthalhydrazide A functionality by treating with hydrazine, forming A attached to a B precursor.

125. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 124 wherein the A-linked diarylketene is further reacted by condensation of two A-linked diarylketenes with an orthoester to form A-B.

126. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 125 wherein condensing reagent is triethylorthoformate.

127. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 126 wherein the A-linked diarylketene comprises at least one of the formula



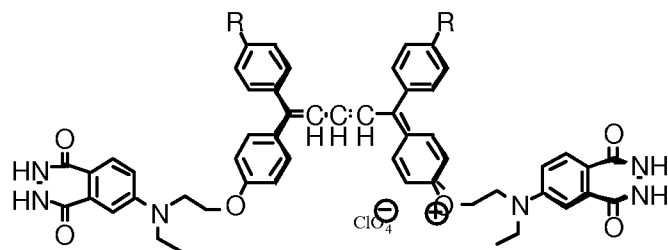
18a: R=OCH₃

18b: R=O(CH₂)₃CH₃

18c: R=(CH₂)₃CH₃

18d: R=N(CH₃)₂

and A-B comprises at least one of the formula



20a: R=OCH₃

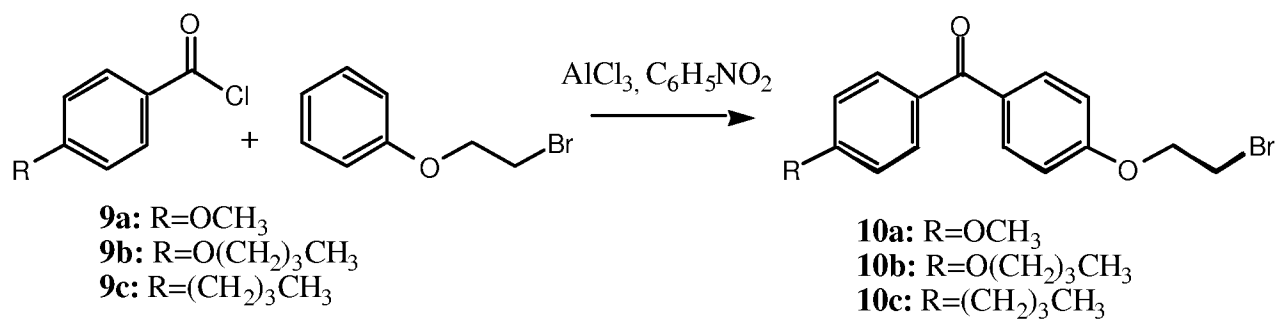
20b: R=O(CH₂)₃CH₃

20c: R=(CH₂)₃CH₃

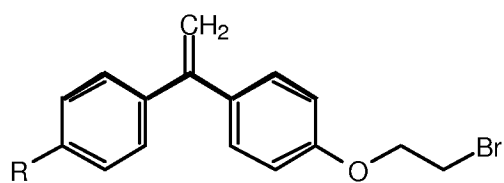
20d: R=N(CH₃)₂

128. (Currently Amended) The method of ~~synthesis of the compound according to any one of~~ claim[[s]] 123 ~~and or~~ or 125 further comprising the step of reacting the B functionality with one nucleophilic species of a C functionality such as Foscarnet to form A-B-C.

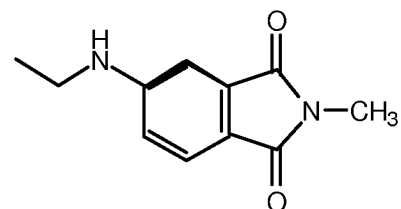
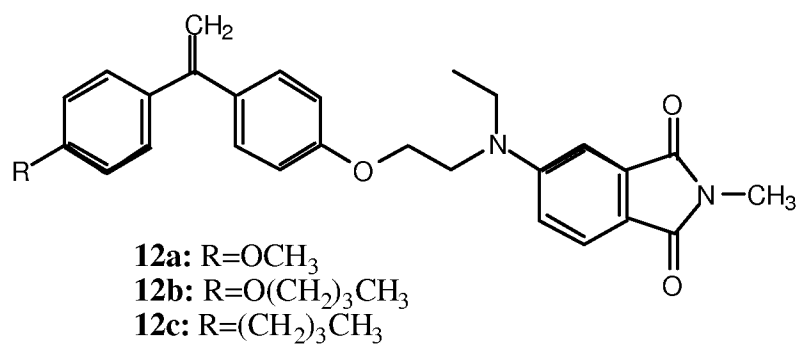
129. (Currently Amended) The method of ~~synthesis of the compound~~ of claim 105 comprising the general steps given by following representative formula

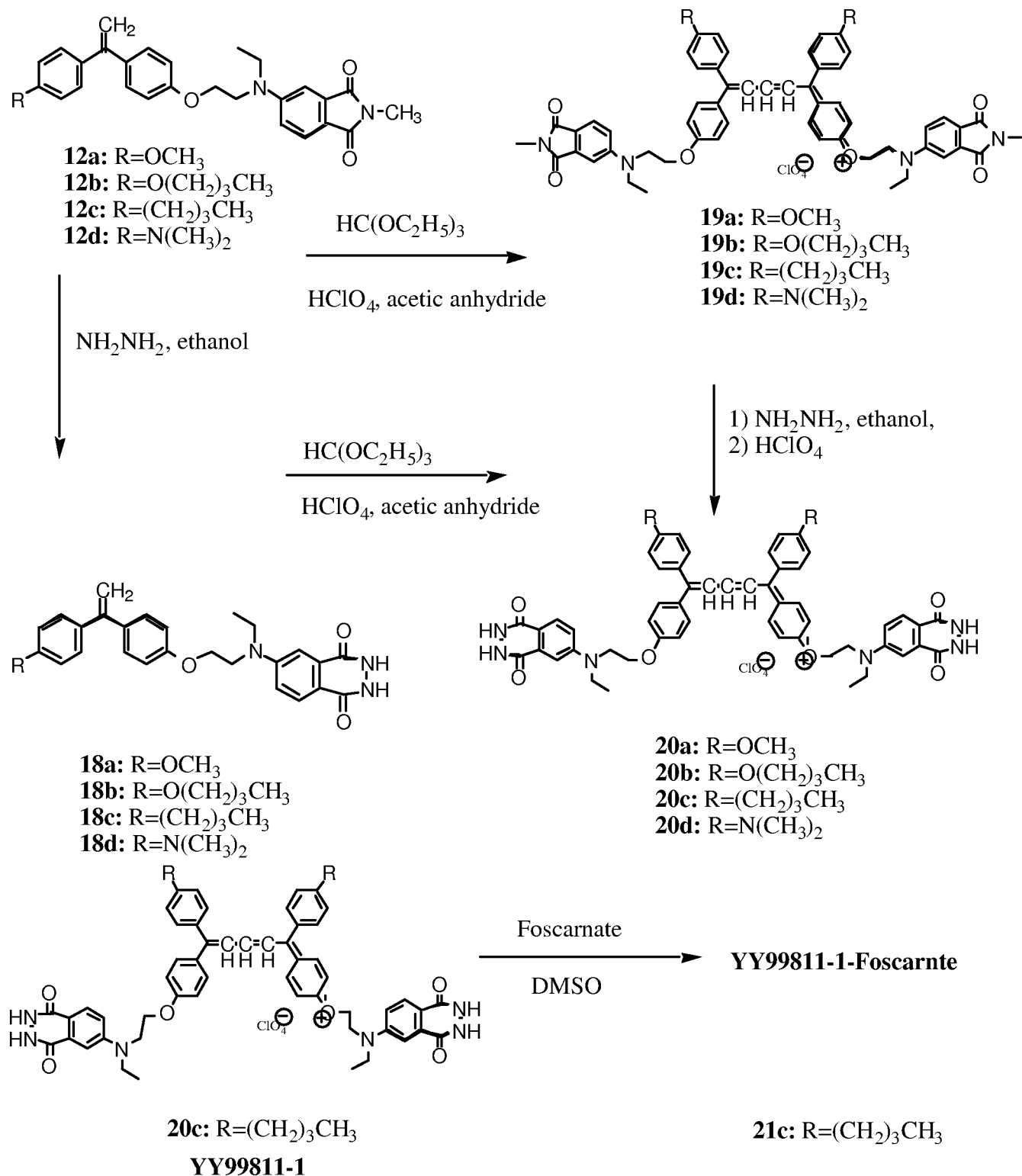
1) CH₃MgBr, benzene

2) HCl



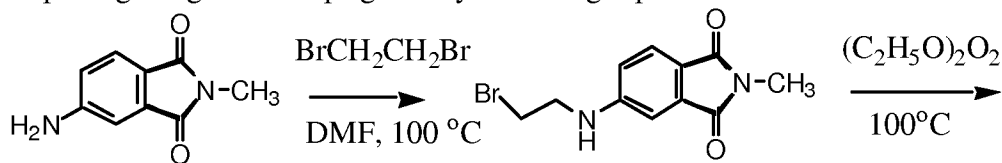
11a: R=OCH₃
11b: R=O(CH₂)₃CH₃
11c: R=(CH₂)₃CH₃

DMF, Na₂CO₃

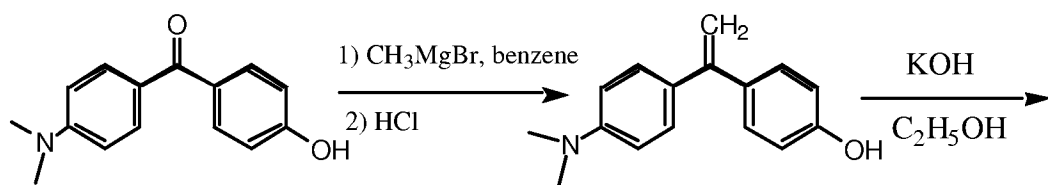
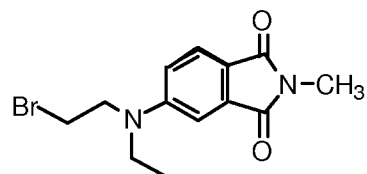


130. (Currently Amended) The method of synthesis of the compound of claim 105

comprising the general steps given by following representative formula



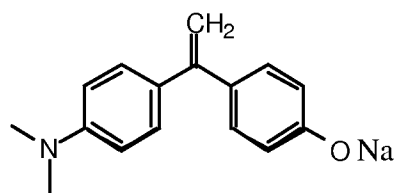
13



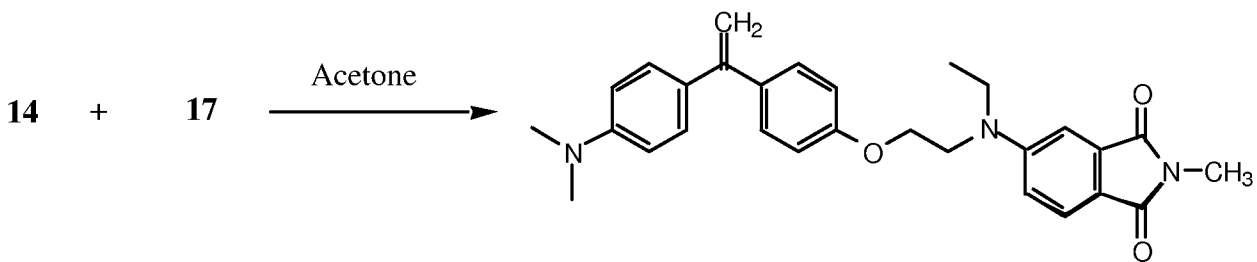
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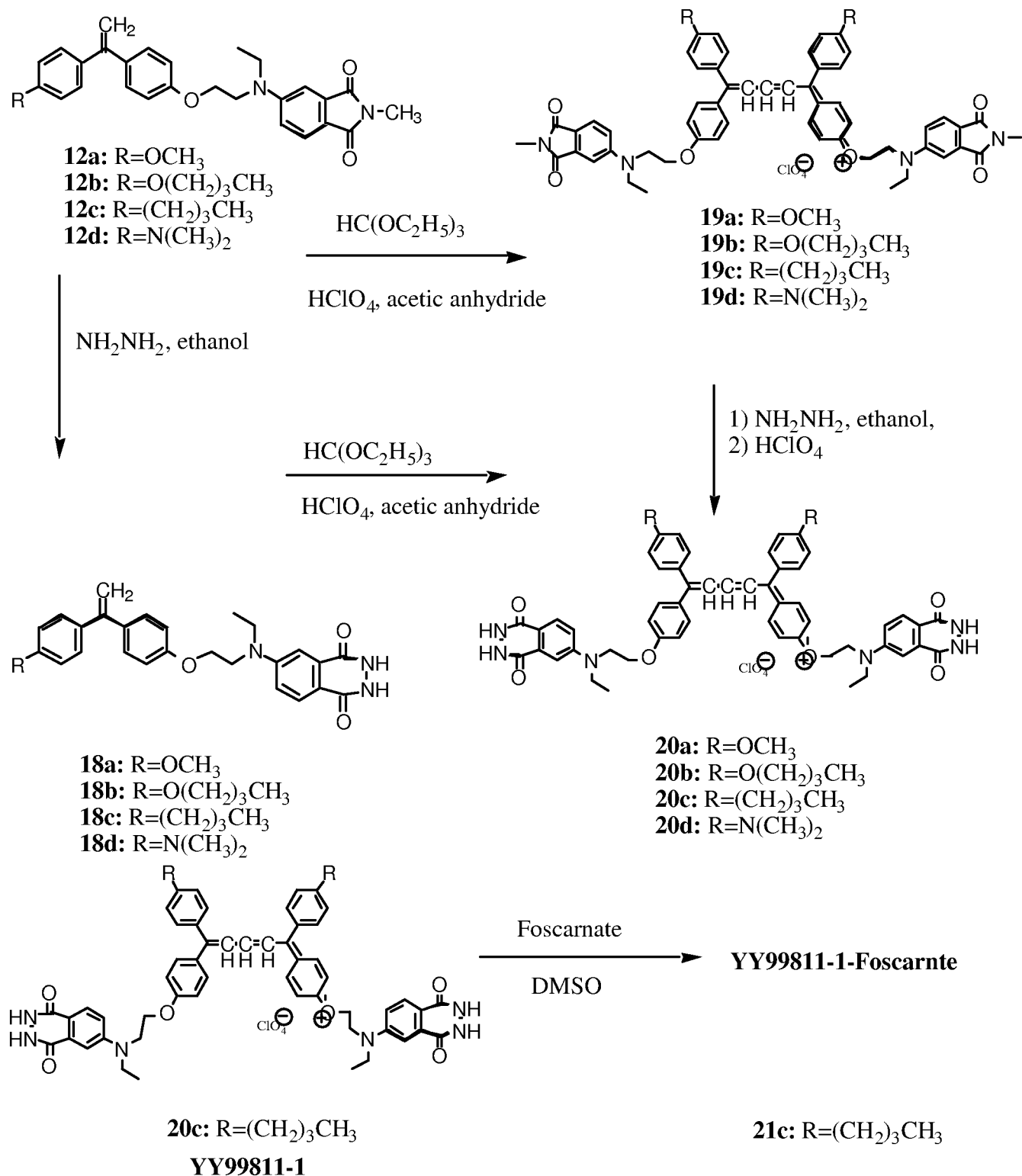
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17



12d



131. (Currently Amended) The method of synthesis of the compound of claim 1 wherein the

A functionality comprises a phthalhydrazide ~~such as a luminol derivative~~ and the B functionality comprises a triarylpolymethine photochromic dye wherein A is attached to aryl groups of B comprising the steps of

- forming a diaryl ketone,
- forming a diaryl ketene from the diaryl ketone,
- forming a protected aminophthalhydrazide such as aminophthalimide or aminophthalic acid diester,
- adding a hydrocarbon linker to the protected aminophthalhydrazide, and
- attaching the protected aminophthalhydrazide through the molecular linker to the aryl groups of diarylketene to form the precursor aminophthalimide-linked diarylketene, and reacting according to at least one of
 - (a) forming the A functionality from the precursor, and condensing the A-linked diarylketene with an aryl alkene aldehyde to form A-B, and
 - (b) condensing the precursor aminophthalimide-linked diarylketene with an aryl alkene aldehyde to form A precursor linked to B, andforming the A functionality from the A precursor to form A-B.

132. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 131 wherein the diaryl ketone is formed by a classical Friedel-Crafts acylation between a benzoyl halide and aryl compound with a hydrocarbon linker having a leaving group.

133. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 132 wherein the aryl compound with a hydrocarbon linker having a leaving group comprises at least one of a halogenated-alkyl-aryl ether and a halogenated-aklyl-aryl amine wherein the halogen is the leaving group.

134. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 133 wherein the halogenated-alkyl-aryl ether comprises 2-bromoethoxybenzene to give an aryl ketone such as 4-(2-bromoethoxy)benzophenone.

135. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 133 wherein the halogenated-aklyl-aryl amine comprises 2-bromoethyl aminobenzene to give an aryl ketone such as 4-(2-bromoethyl amino)benzophenone.

136. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 131 wherein the diaryl ketone is converted to the corresponding diarylketene by reacting with a methylating

reagent such as a methyl Grignard reagent, methyl lithium reagent, lithium dimethylcopper reagent and then dehydration with acid.

137. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 136 wherein the diaryl ketone is converted to the corresponding diarylketene by reacting with methylmagnesium bromide and then dehydration with acid.

138. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 131 wherein the diaryl ketone is converted to the corresponding diarylketene by a Wittig reaction.

139. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 131 wherein a linker is attached to the protected aminophthalhydrazide by a reaction of a nucleophilic group of the linker or protected aminophthalhydrazide with a leaving group of the linker or protected aminophthalhydrazide.

140. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 131 wherein a linker is attached to the protected aminophthalhydrazide by reaction to form a bond between at least one of a nitrogen, oxygen, or carbon atom of the linker and at least one of a nitrogen, oxygen, or carbon atom of group of the protected aminophthalhydrazide by an addition or a substitution reaction of a leaving group.

141. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 140 wherein a linker is attached to the protected aminophthalhydrazide by a substitution reaction of at least one of a halogen, tosylate group, ester group with a nitrogen, oxygen, or carbon atom.

142. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 131 wherein attaching the protected aminophthalhydrazide through the molecular linker to one of the aryl groups of diarylketene to form the precursor aminophthalimide-linked diarylketene is by a reaction of a nucleophilic group of the linker or aryl group of diarylketene with a leaving group of the linker or aryl group of diarylketene.

143. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 142 wherein a linker is attached to the aryl group of diarylketene by reaction to form a bond between at least one of a nitrogen, oxygen, or carbon atom of the linker and at least one of a nitrogen, oxygen, or carbon atom of group of the protected aminophthalhydrazide by an addition or a substitution reaction of a leaving group.

144. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 143 wherein a linker is attached to the aryl group of diarylketene by a substitution reaction of at least one of a halogen, tosylate group, ester group with a nitrogen, oxygen, or carbon atom.

145. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 131 wherein the precursor aminophthalimide-linked diarylketene is further reacted by condensation with an aryl alkene aldehyde in a nonaqueous solvent, containing an acid catalyst to form B linked to the A precursor.

146. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 145 wherein the precursor aminophthalimide-linked diarylketene is an aminophthalimide-substituted 1,1-diarylethene,

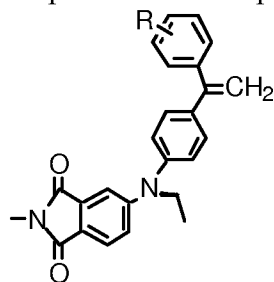
the aryl alkene aldehyde is a p-aminophenyl alkene aldehyde such as p-(dimethylamino)-cinnamaldehyde,

the nonaqueous solvent is acetic anhydride,

the acid catalyst is at least one of perchloric acid and tetrafluoroboric acid, and

the B linked to the A precursor comprises a aminophthalimide-substituted multiarylpolymethine dye.

147. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 145 wherein the precursor aminophthalimide-linked diarylketene comprises at least one of the formula



3a: R = N(CH₃)₂

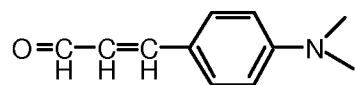
3b: R = H

3c: R = OCH₃

3d: R = O(CH₂)₃CH₃

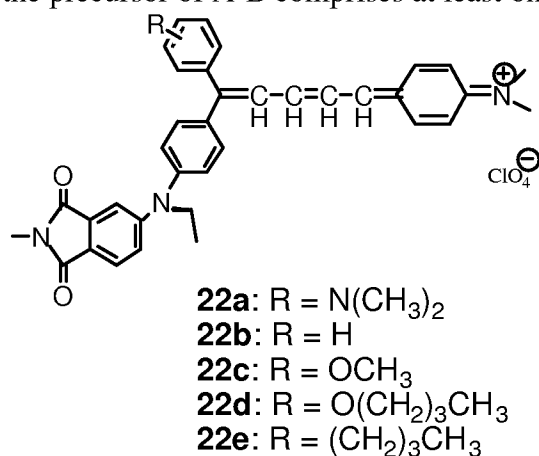
3e: R = (CH₂)₃CH₃ ,

the aryl alkene aldehyde has the formula



4-(Dimethylamino)cinnamaldehyde, and

the precursor of A-B comprises at least one of the formula



148. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 145 wherein the phthalimide moiety of the A precursor is converted to the phthalhydrazide A functionality by treating with hydrazine, forming A-B.

149. (Currently Amended) The method ~~of synthesis of the compound~~ of claims 148 wherein the B functionality is protected by reacting with an anion such as hydroxide, methoxide and amine, the A-B precursor is refluxed with hydrazine in a suitable solvent such as an alcoholic solvent in inert atmosphere and then treated with acid such as perchloric acid, tetrafluoroboric acid to form A-B.

150. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 131 wherein the phthalimide moiety of the A precursor of the precursor aminophthalimide-linked diarylketene is converted to the phthalhydrazide A functionality by treating with hydrazine, forming A attached to a B precursor.

151. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 150 wherein the A-linked diarylketene is further reacted by condensation with an aryl alkene aldehyde in a nonaqueous solvent, containing an acid catalyst to form A-B.

152. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 151 wherein the A-linked diarylketene is an aminophthalhydrazide-substituted 1,1-diarylethene,

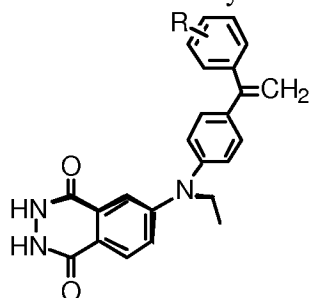
the aryl alkene aldehyde is a p-aminophenyl alkene aldehyde such as p-(dimethylamino)-cinnamaldehyde,

the nonaqueous solvent is acetic anhydride,

the acid catalyst is at least one of perchloric acid and tetrafluoroboric acid, and

A-B comprises a aminophthalhydrazide-substituted multiarylpolymethine dye.

153. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 152 wherein the A-linked diarylketene comprises at least one of the formula



3a: R = N(CH₃)₂

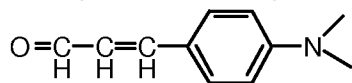
3b: R = H

3c: R = OCH₃

3d: R = O(CH₂)₃CH₃

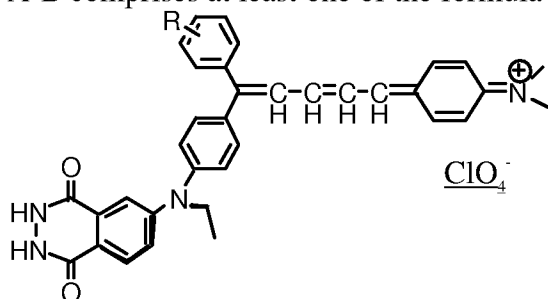
3e: R = (CH₂)₃CH₃

the aryl alkene aldehyde has the formula



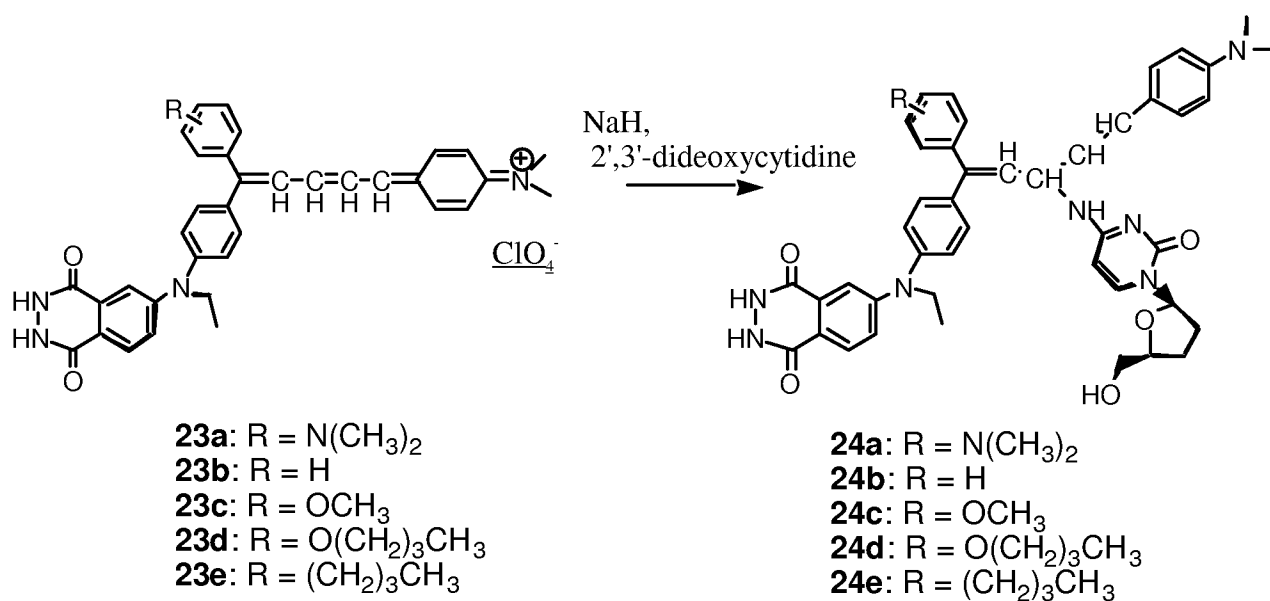
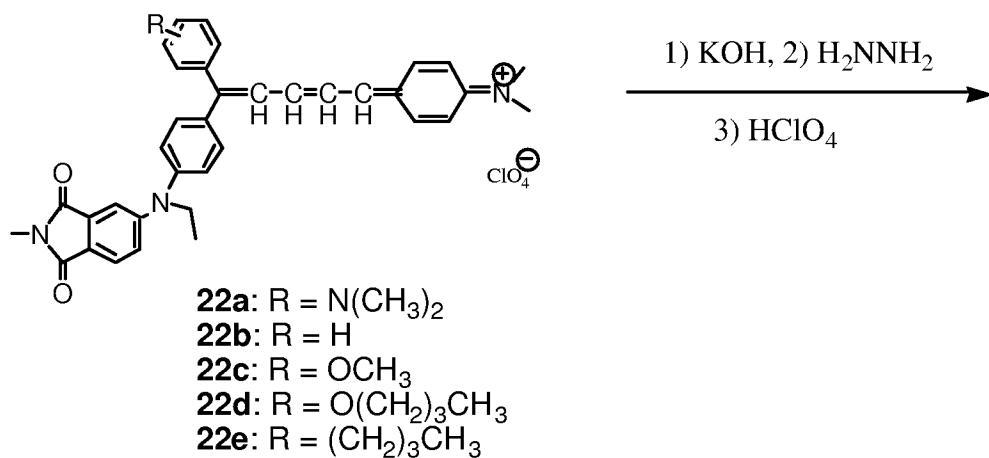
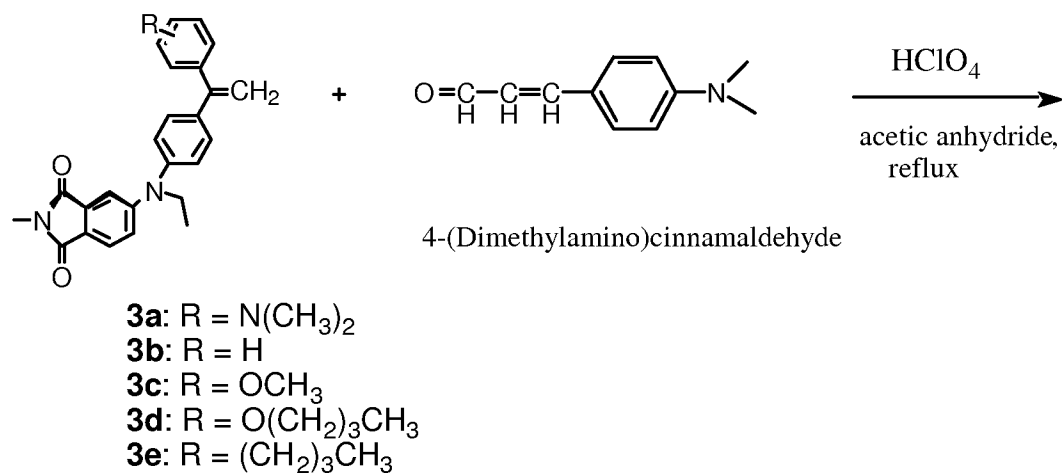
4-(Dimethylamino)cinnamaldehyde, and

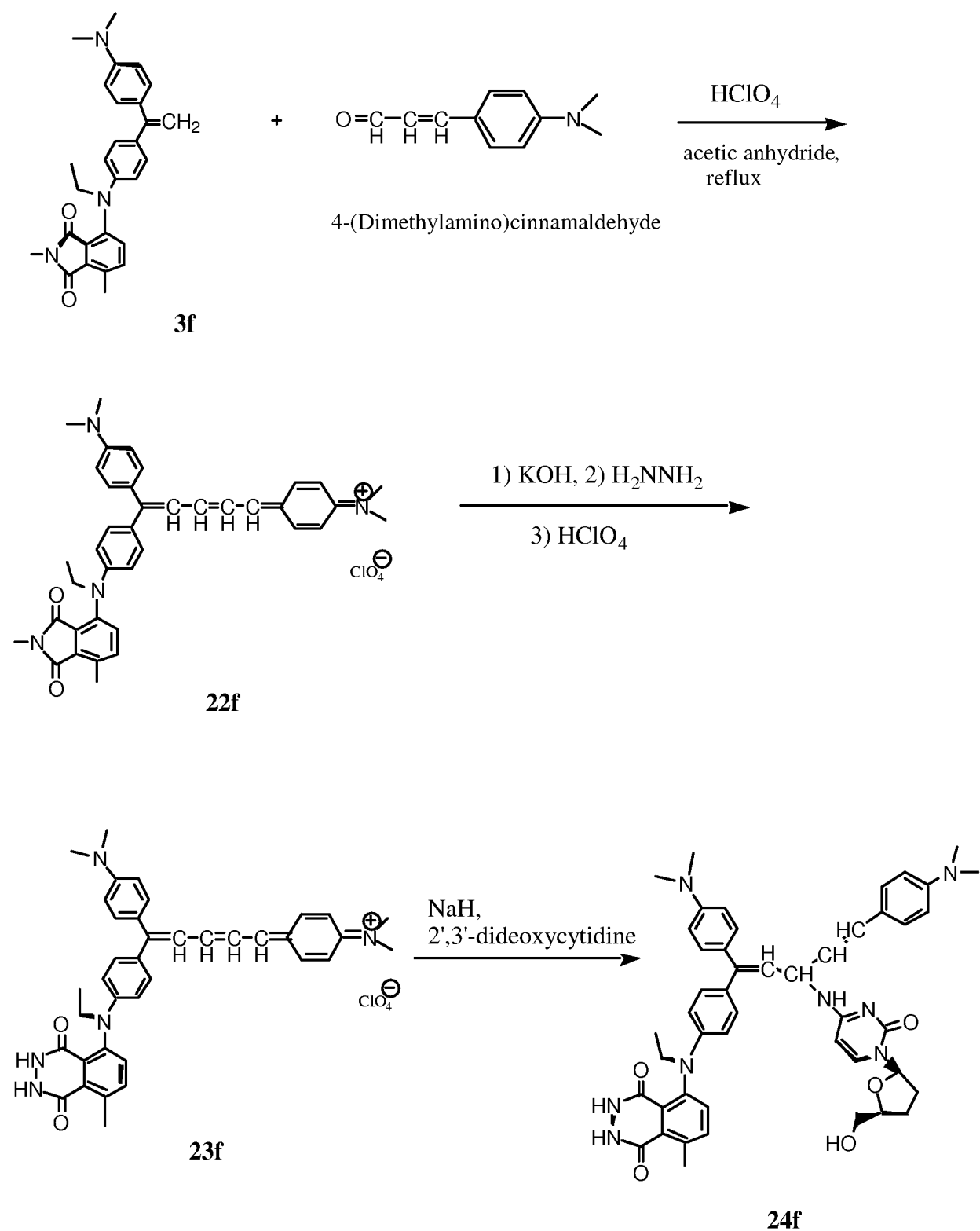
A-B comprises at least one of the formula



154. (Currently Amended) The method of ~~synthesis of the compound according to any one of~~ claim[[s]] 149 ~~and~~ or 151 further comprising the step of reacting the B functionality with one nucleophilic species of a C functionality such as Foscarnet to form A-B-C.

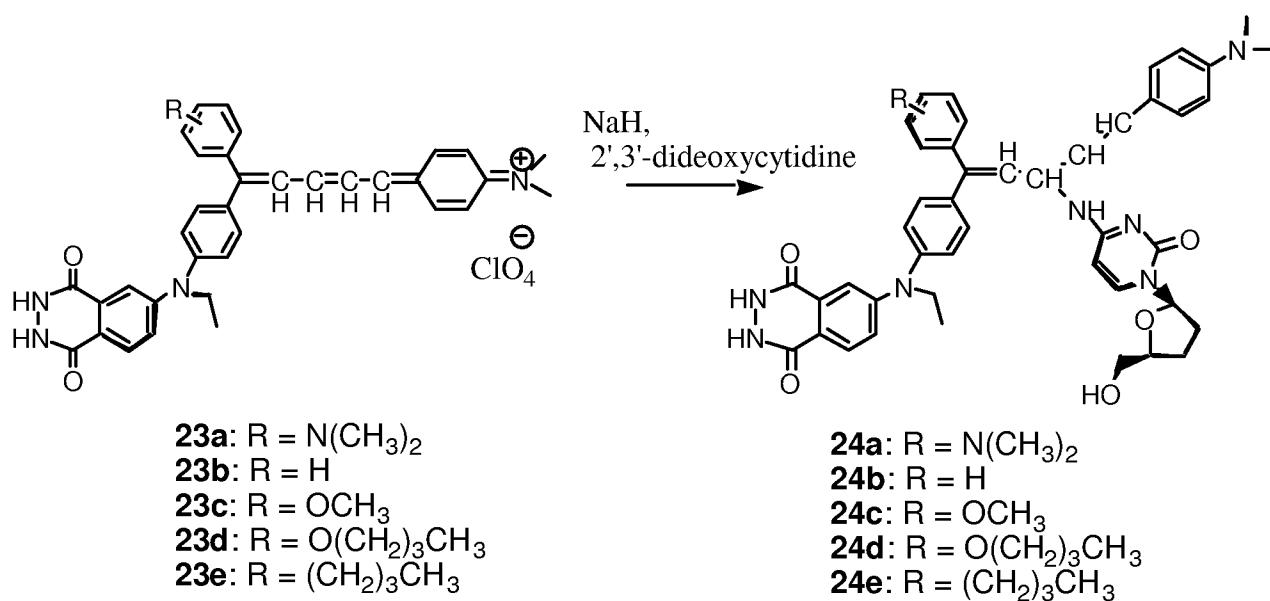
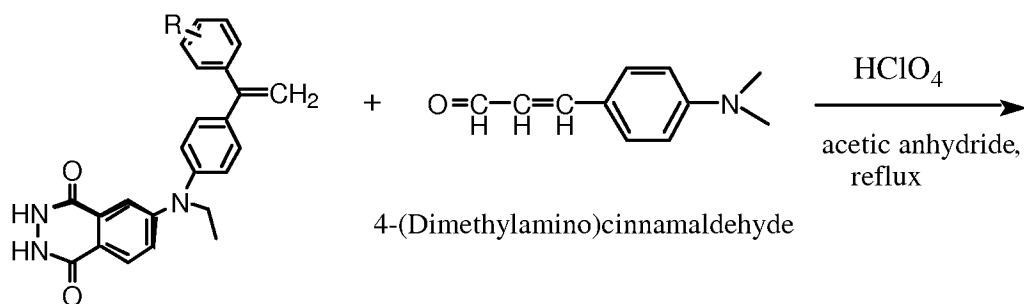
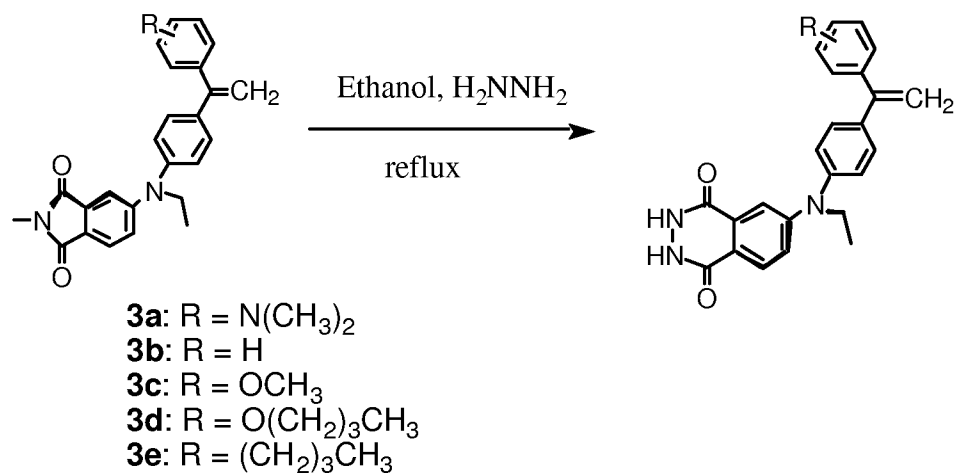
155. (Currently Amended) The method of ~~synthesis of the compound~~ of claim 131 comprising the general steps given by following representative formula

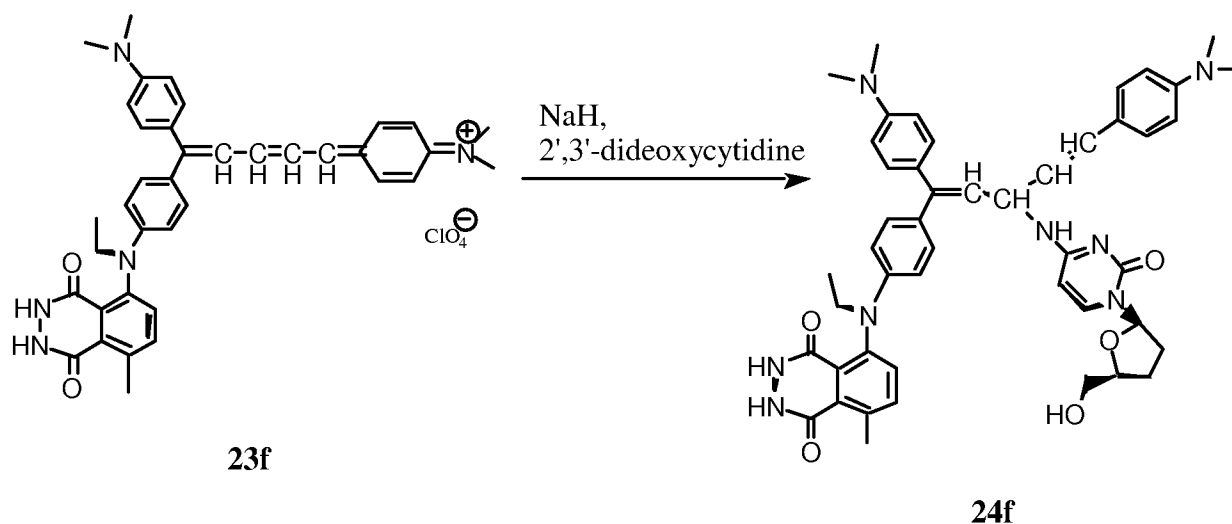
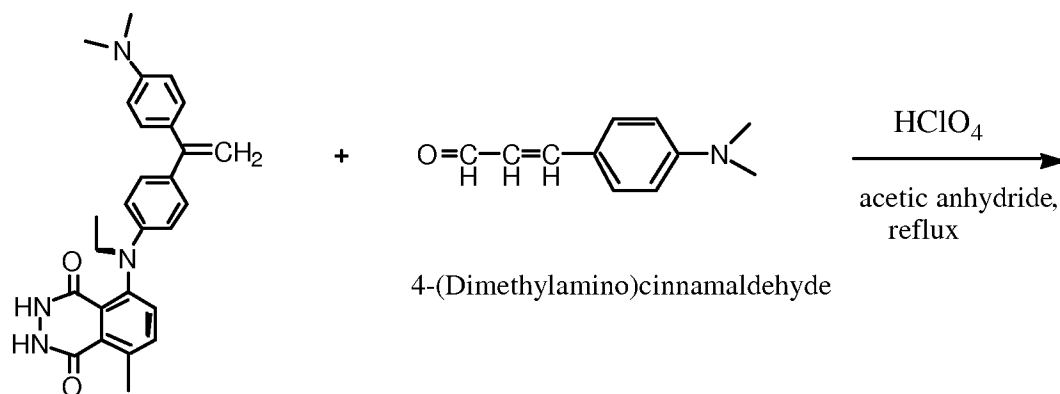
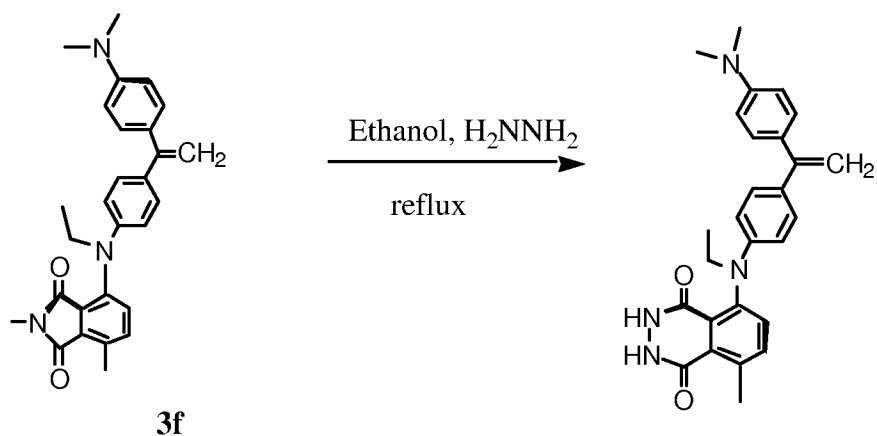




156. (Currently Amended) The method of synthesis of the compound of claim 131

comprising the general steps given by following representative formula





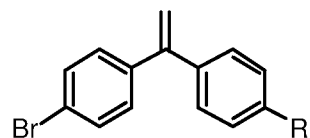
157. (Currently Amended) The method of synthesis of the compound of claim 1 wherein the

A functionality comprises a phthalhydrazide ~~such as a luminol derivative~~ and the B functionality comprises a triarylpolymethine photochromic dye wherein A is attached to aryl groups of B comprising the steps of

- forming a diaryl ketone,
- forming a diaryl ketene from the diaryl ketone,
- condensing the diarylketene with an aryl alkene aldehyde to form B
- forming a protected aminophthalhydrazide such as aminophthalimide or aminophthalic acid diester,
- adding a hydrocarbon linker to the protected aminophthalhydrazide, and
- attaching the protected aminophthalhydrazide through the molecular linker to the aryl groups of B to form the precursor aminophthalimide-linked B, and
- forming the A functionality from the precursor to form A-B.

158. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 157 wherein at least one of the diaryl ketone and diarylketene is halo-substituted and the protected aminophthalhydrazide is attached through the linker by an amination reaction.

159. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 158 wherein the halo-substituted diarylketene precursor compounds comprises the formula of at least one of



2a: R = N(CH₃)₂

2b: R = H

2c: R = OCH₃

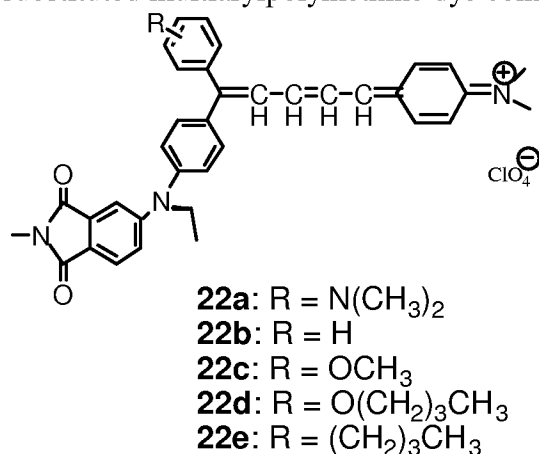
2d: R = O(CH₂)₃CH₃

2e: R = (CH₂)₃CH₃, and

the halo-substituted multiarylpolymethine dyes, such as 1-(p-bromophenyl)-1,5-bis(p-dimethylaminophenyl)-pentadienium perchlorate, are prepared by condensation with a p-aminophenyl alkene aldehyde such as p-(dimethylamino)cinnamaldehyde.

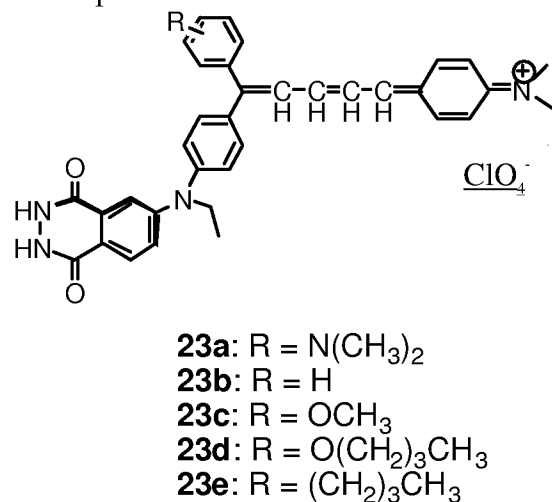
160. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 158 wherein B is protected by reacting with an anion such as alkoxide and then coupled with A by amination of aryl halide such as the palladium-catalyzed amination of aryl halide to obtain the alkoxide-protected aminophthalimide-substituted multiarylpolymethine dye.

161. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 160 wherein the protected aminophthalhydrazide-linked to B from the alkoxide-protected aminophthalimide-substituted multiarylpolymethine dye comprises at least one of the formula



162. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 160 wherein the alkoxide-protected aminophthalimide-substituted multiarylpolymethine dye is refluxed with hydrazine in a suitable solvent such as an alcoholic solvent to convert the amino-phthalimide moiety to the aminophthalhydrazide moiety and then treated with acid to generate A-B.

163. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 162 wherein A-B comprises at least one of the formula



164. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 162 further comprising the step of reacting the B functionality with one nucleophilic species of a C functionality such as Foscanet to form A-B-C.

165. (Currently Amended) The method of ~~synthesis of the compound~~ of claim 157 wherein at least one of the diaryl ketone and diarylketene is halo-substituted and an aminophthalhydrazide is attached through the linker by an amination reaction.

166. (Currently Amended) ~~[[A]]The method of claim 20, synthesis of a compound having the formula A-B-C~~

~~wherein the~~ A is a chemiluminescent moiety comprising an active oxalate; and

B is an energy acceptor moiety comprising a multiarylpolymethine photochromic dye; and

~~—C is a biologically active moiety;~~

~~wherein the chemiluminescent moiety A comprises an active oxalate and the energy acceptor moiety B comprises a multiarylpolymethine photochromic dye wherein the chemiluminescent moiety A is attached to aryl groups of the energy acceptor moiety B comprising the steps of~~

~~forming a halo-substituted diaryl ketone,~~

~~forming a halo-substituted diaryl ketene from the diaryl ketone,~~

~~amination of the halo-substituted diaryl ketene to give amino-diarylketene,~~

~~substitution at the amino-group of the ketene to forming the corresponding sulfonamide,~~

~~condensing the sulfonamide with a catalyst, and~~

~~react with oxalyl halide to form A-B.~~

167. (Currently Amended) ~~[[A]]The method of claim 20, synthesis of a compound having the formula A-B-C~~

~~wherein the~~ A is a chemiluminescent moiety comprising a cyclized active oxalate; and

B is an energy acceptor moiety comprising a multiarylpolymethine photochromic dye; and

~~—C is a biologically active moiety comprising a nucleophilic moiety;~~

~~wherein the chemiluminescent moiety A comprises an cyclized active oxalate and the energy acceptor moiety B comprises a multiarylpolymethine photochromic dye wherein chemiluminescent moiety A is attached to aryl groups of the energy acceptor moiety B comprising the steps of~~

~~forming a halo-substituted diaryl ketone,~~

~~forming a halo-substituted diaryl ketene from the diaryl ketone,~~

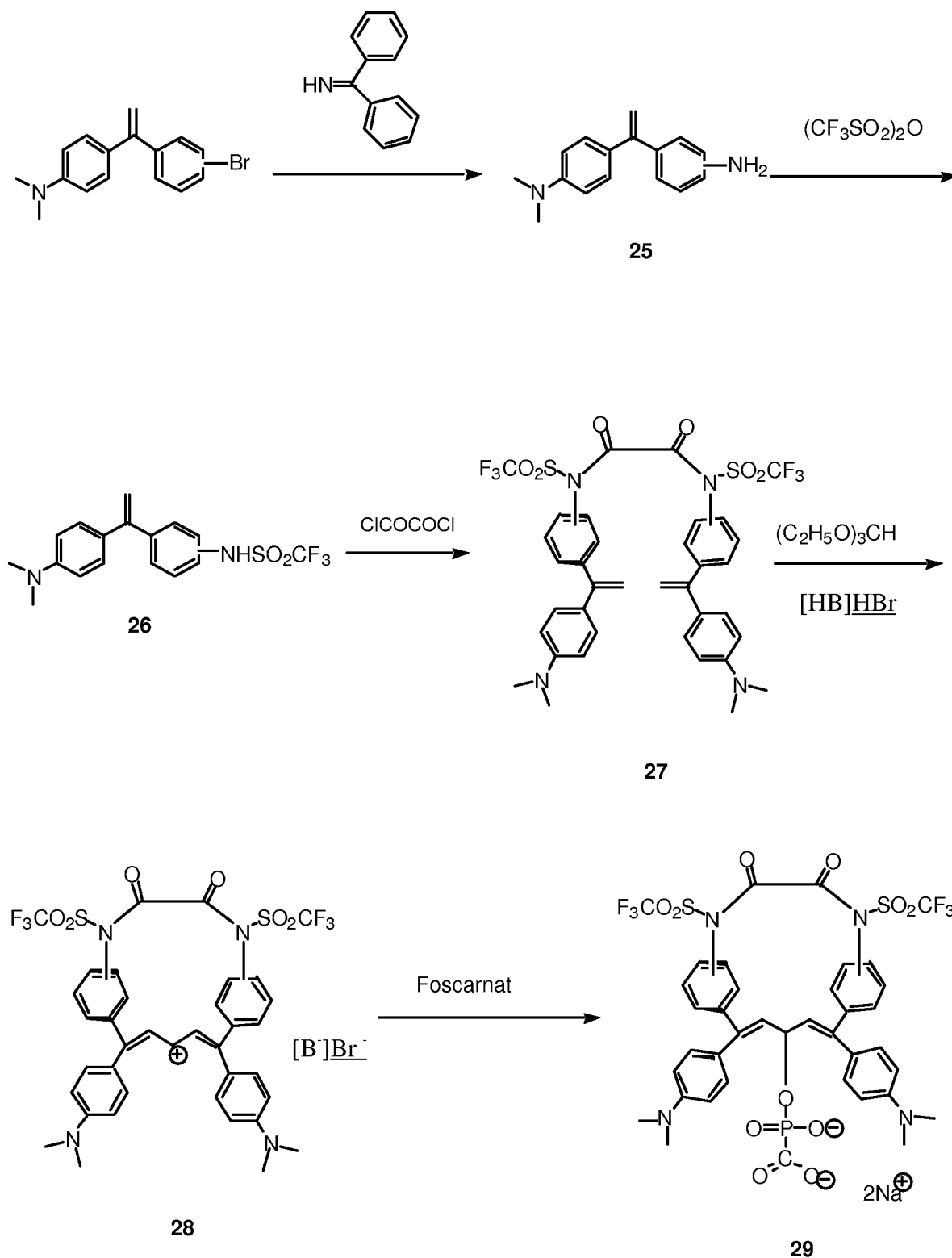
~~amination of the halo-substituted diaryl ketene to give amino-diarylketene,~~

~~substitution at the amino-group of the ketene to forming the corresponding sulfonamide,~~

~~reacting 2 molar proportions of a *N*-substituted aminodiarylketene with 1 molar oxalyl halide to yield the *N,N'*-bisaryl oxamide, and
condensing the oxamide with a catalyst to form A-B.~~

168-171. (Cancelled)

172. (Currently Amended) ~~The method of synthesis of the compound of claim 167, comprising the following steps wherein the general steps are given by following representative formula~~



173. (Currently Amended) The method of synthesis of the compound of claim [[1]]20

wherein the chemiluminescent moiety A comprises an active oxalate and the energy acceptor moiety B comprises a multiarylpolymethine photochromic dye wherein the chemiluminescent moiety A is attached to aryl groups of the energy acceptor moiety B through a molecular linker comprising the steps of

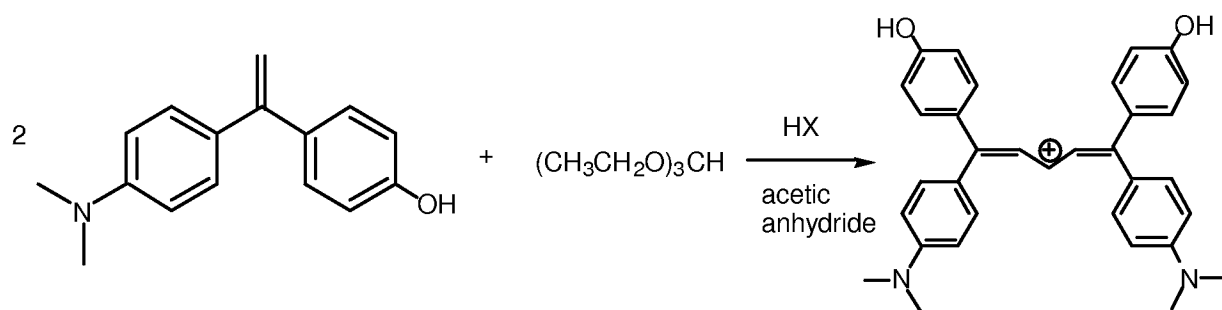
- forming B comprising a functionalized tetraarylpolymethine dye,
- reacting a substituted amine with a sulfonyl anhydride to form a substituted alkyl sulfonamide,
- reacting the substituted alkyl sulfonamide with an oxalyl ~~chloride~~derivative to form a substituted oxamide,
- reacting the substituted oxamide with the functionalized tetraarylpolymethine dye to form A-B comprising a cyclized oxamido-tetraarylpolymethine.

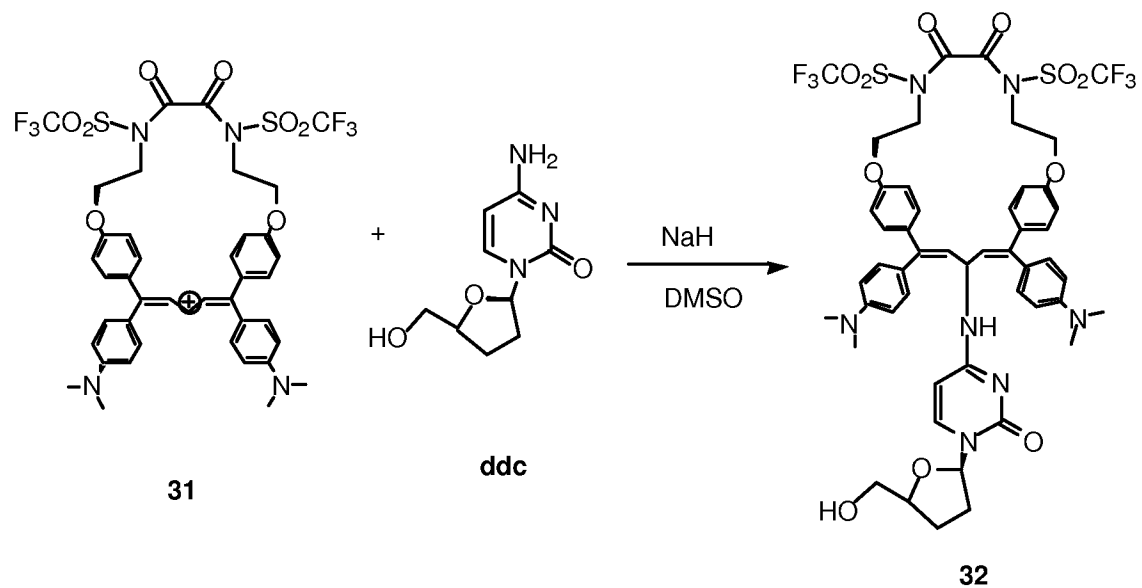
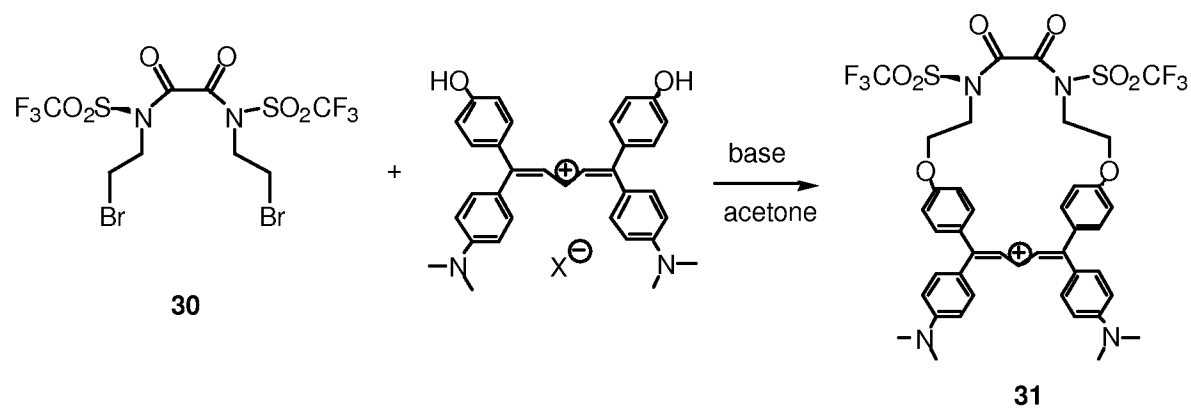
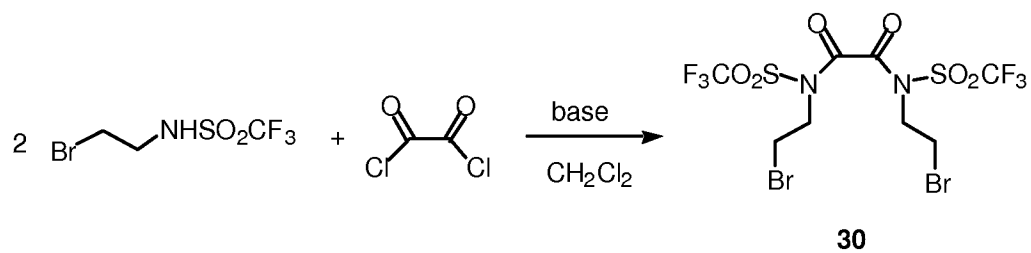
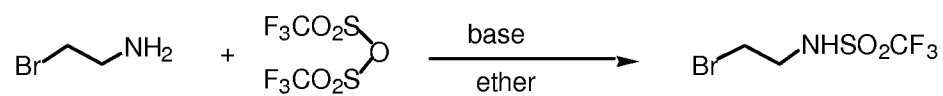
174. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 173 wherein the substituted amine is N-2-bromoethylsulfamide.

175-179. (Cancelled)

180. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 173 further comprising the step of reacting the B functionality with one nucleophilic species of a C functionality such as Foscarnet to form A-B-C.

181. (Currently Amended) The method ~~of synthesis of the compound~~ of claim 173 comprising the general steps given by following representative formula





Claims 182-227 (Cancelled)

228. (Currently Amended) The method of synthesis of the compound of claim 10 wherein the C moiety is at least one ~~or a derivative or analog~~ of one of the group of

- prostaglandins,
- prostaglandin A, A₁, A₂, B, B₁, E, E₁, E₂, F, or F₁, ~~or an analog which possesses a vasodilatory effect on coronary arteries and other human vascular beds~~
- ~~prostaglandin E, F, A or an analog which possesses a positive cardiac inotropic effect~~
- ~~prostaglandin A, E, or an analogue prostaglandin which possesses natriuretic and diuretic activity~~
- ~~prostaglandin A, G, E₁, E₂, or an analogue such as 15(S)-15-methyl PGE 2 methylester, 16,16-dimethyl PGE₂, AY-22,093, AY22,469, AY-22,443, or 15(R)-15-methyl PGE₂, which inhibits gastric acid secretion~~
- ~~prostaglandin D₂, E₁ or an analogue which inhibits platelet aggregation~~
- ~~prostaglandin E₁, E₂ or an analogue which causes bronchial dilatation~~
- ~~prostaglandin F₂ or an analogue which causes abortion by luteolysis~~
- ~~prostaglandin A₂, E₁, E₂, or an analogue which induces erythropoiesis~~
- ~~prostaglandin E or an analogue which modulates T lymphocytes to decrease their ability to reject an allogenic graft~~
- 2'-isopropyl-4'-(trimethylammonium chloride)-5'-methylphenyl piperidine -1-carboxylate (Amo 1618), ~~or an analog which inhibits the cyclization of trans geranyl geranyl PP to copalyl-PP during Kaurene synthesis~~
- adenosine cyclic 3', 5'-monophosphate, ~~or an analogue which inhibits the release and formation of phlogistic mediators such as histamine and kinins~~
- 4'-sulfamylphenyl,
- 2-azo -7-acetamid-1-hydroxynaphthalene-3,6-disulfonate (Neoprontosil), 4'-sulfamyl-2, 4-diaminoazobenzene (Prontosil), or 5-(p-sulfamylphenylazo) salicylic acid (Lutazol), ~~or analog which possess potent carbonic acid anhydrase inhibition~~
- ~~analogue of S-adenosyl homocysteine or sinefungin~~
- phosphoglycolohydroxamate which inhibits Class II aldolases present in bacterial and fungi and is noninhibitory of Class I aldolases present in animals,
- inosine analogue such as or formycin B, ~~which inhibits nucleotide phosphorylase during nucleotide metabolism~~
- phosphonoformate (Foscarnet), ~~or an analog which inhibits the HIV reverse transcriptase enzyme~~
- \square -amino-butyric acid (GABA), ~~or an analog which is the major inhibitory~~

~~neurotransmitter in the mammalian central nervous system~~

~~gabaculine, N-(5'-phosphopyridoxyl)-4-aminobutyric acid, ethanolamine-o-sulfate, γ -vinyl GABA, or γ -acetylenic GABA, or an analog that is an inhibitor of the GABA degrading enzyme, GABA: 2-oxoglutarate aminotransferase~~

Baclofen or a compound that inhibits GABA release,

an oligonucleotide which binds to RNA or DNA and blocks transcription or translation of HIV or P-glycoprotein gene products adenosine which binds to brain purinergic receptors to suppress opiate withdrawal,

adenosine which causes coronary vasodilatation,

3-hydroxy-3-methylglutarate, 3-hydroxybutyrate, 3-hydroxy-3-methylpentanoate, 4-bromocrotonyl-CoA, but-3-ynoyl-CoA, pent-3-ynoyl-CoA, dec-3-ynoyl-CoA, ML-236A, ML-236B (compactin), ML-236C, mevinolin, mevinolinic acid, ~~or a mevalonic acid analogue which is an inhibitor of 3-hydroxy-3-methylglutaryl-CoA reductase which catalyzes the rate limiting and irreversible step of cholesterol synthesis where inhibition at this step does not lead to the accumulation of nonmetabolizable precursors~~

thioinosinate which suppresses T lymphocytes,

Suramin, which is a powerful inhibitor of energy driven calcium uptake by the sarcoplasmic reticulum and is an intracellular inhibitor of Na⁺ K⁺ ATPase where both activities increase intracellular calcium concentrations with a concomitant inotropic effect,

norepinephrine N-methyltransferase inhibitor such as 2,3-dichloro- γ -methylbenzylamine, 2,3-dichlorobenzylamine, 2,3-dichlorobenzamidine, or 3,4-dichlorophenylacetamidine,

~~adenosine cyclic 3', 5'-monophosphate or a cAMP analogue which blocks the synthesis of fatty acids and cholesterol in the liver is an antilipidemic agent,~~

an inhibitor of dihydroxyphenylalanine decarboxylase during the synthesis of epinephrine and norepinephrine such as psitectorigenin, genistein, 3', 4', 5, 7-tetrahydroxy-8-methylisoflavone, orbol, 8-hydroxygenistein, 3', 5, 7-trihydroxy-4', 6-dimethylisoflavone, 3', 5, 7-trihydroxy-4', 8-dimethoxyisoflavone, D,L-B-(5-hydroxy-3-indolyl)- γ -hydrazinopropionic acid, D,L- γ -hydrazino- γ -methyl-dopa, D,L-B-(3-indolyl)- γ -hydrazinopropionic acid, ~~a derivative of phenylalanine such as~~ N-methyl-3,4-dopa, γ -acetamido-3,4-dimethoxycinnamic acid, DL- γ -methyl-3,4-dopa, γ -methyl-B-(3-hydroxy-4-methoxyphenyl)alanine, γ -methyl-3,4-dimethoxyphenylalanine, or d-catechin; D,L-B-(3-indolyl)- γ -methyl- γ -hydrazinopropionic acid (R)-3,3,4-dihydroxyphenyl-1-fluoropropylamine, (S)- γ -fluoromethyl-dopa, (S)- γ -fluoromethyltyrosine, 5-(3,4-dihydroxycinnamoyl) salicylic acid, 3-hydroxycinnamic acid, caffeic acid, 3-mercaptocinnamic acid, γ -methyl-3-hydroxycinnamic acid, γ -ethyl-3-hydroxycinnamic acid, 3-hydroxy-w-nitrostyrene, 3,4-dihydroxyhydrocinnamic acid, 3-hydroxybenzalacetone, 3-hydroxychalcone, 3-hydroxybenzal furanyl ketone, 3-hydroxybenzal

thiophenyl ketone, 3',4'-dihydroxyflavone, 8-O-glucoseflavone, flavone, 3-hydroxyphenyl pyruvic acid, 3,4-dihydroxyphenylpyruvic acid phenylthiopyruvic acid, 4-hydroxyphenylpyruvic acid, dithiosalicylic acid, 1-hydroxy-2-naphthoic acid, 3-hydroxy-7-sulfo-2-naphthoic acid, 3,5-dihydroxy-2-naphthoic acid, 4-chlorocinnamic acid, 2-chlorocinnamic acid, 2,4-dichlorocinnamic acid, 3-nitrocinnamic acid, 3,5-dibromo-2-hydroxycinnamic acid, 2,4,6-triiodo-3-hydroxycinnamic acid, 2-hydroxy-4'-cyanochalcone, 4-(4-hydroxycinnamoyl) benzonitrile, 2-(4-hydroxycinnamoyl)-1,4-dihydroxybenzene, quercetin-6'-sulfonic acid, 5-(2-hydroxy-3,5-dibromocinnamoyl) salicylic acid or 5-(3-hydroxycinnamoyl) salicylic acid,

an inhibitor of acrosin, a proteolytic enzyme located in the acrosome of sperm, such as tosyl lysine chloromethyl ketone, N- α -tosyl-L-arginine chloromethyl ketone, or ethyl p-guanidinobenzoate,

adenosine cyclic 3',5'-monophosphate (cAMP), N⁶, O₂-dibutyryl-adenosine cyclic 3',5'-monophosphate ~~or an analogue which produces an inotropic response,~~

adenosine kinase enzyme inhibitor such as 6,6'-dithiobis (9-B-D-ribofuranosylpurine),

inhibitor of monoamine oxidase such as phenylhydrazine, phenylethylidenehydrazine, isopropylhydrazine, or iproniazid,

an inhibitor of catechol-o-methyltransferase such as 3,5-diiodo-4-hydroxybenzoic acid, S-3'-deoxyadenosyl-L-homocysteine, pyrogallol, R04-4602, gallic acid, 3,5-dihydroxy-4-methylbenzoic acid, 1,3-dihydroxy-2-methoxybenzene, 1-hydroxy-2,3-dimethoxybenzene, 2-hydroxy-1,3-dimethoxybenzene, 1,3-dihydroxy-4-methoxybenzene, catechol, 3,4-dihydroxybenzoic acid, caffeic acid, 5,6-dihydroxyindole, noradrenaline, dopacetamide, H 22/54, quercetin, nordihydroguaiaretic acid, U-0521, arterenone, methylspinazarin, MK 486, dopa, papaveroline, isoprenaline, 7,8-dihydroxy-chlorpromazine, 3-hydroxy-4-pyridone, tetrahydroisoquinoline pyridoxal 5'-phosphate, iodoacetic acid, 3-mercaptoptyramine, dehydrodicaffeic acid dilactone, methylspinazarin, 3',5,7-trihydroxy-4',6-dimethoxyisoflavone, 3',5,7-trihydroxy-4',8-dimethoxyisoflavone, 6,7-dihydroxymethylspinazarin, S-adenosylhomocysteine, S-tubercidinylhomocysteine, 3',8-dihydroxy-4',6,7-trimethoxyisoflavone, 7-O-methylspinachrome B, 6-(3-hydroxybutyl)-7-O-methylspinachrome B, 3,5-diiodosalicylic acid, or pyridoxal-5'-phosphate,

an inhibitor of adenosine deaminase which blocks the metabolism of adenosine such as coformycin, arabinosyl-6-thiopurine, 6-methylthioinosine, 6-thioinosine, 6-thioguanosine, N₁-methyladenosine, N₆-methyladenosine, 2-fluorodeoxyadenosine, 2-fluoroadenosine, inosine, 2'-deoxyinosine, deoxycoformycin, 1,6-dihydro-6-hydroxymethyl purine ribonucleoside, erythro-9-(2-hydroxy-3-nonyl)adenine, or 9-B-D-arabinofuranosyl-6-hydroxylaminopurine,

an inhibitor of adenylate kinase, 5'-nucleotidase, and adenosine translocase such as p¹ p⁵ - diadenosine pentaphosphate, \square, \square -methylene adenosine diphosphate, and nitrobenzyl-6-

thioinosine, respectively,

an inhibitor of α -aminobutyric acid uptake such as D,L-2,4-diaminobutyric acid, D,L-B-hydroxy GABA, (-)-nipecotic acid, trans-4-aminocrotonic acid, cis-3-aminocyclopentane-1-carboxylic acid, trans-3-aminocyclopentane-1-carboxylic acid, B-guanidinopropionic acid, homohypotaurine, 4-aminopentanoic acid, homotaurine, B-alanine, imidazoleacetic acid, 6-aminohexanoic acid, D,L-carnitine, D,L-2,6-diaminopimetic acid, D,L-2-fluoro GABA, guanidino acetic acid, 2-hydrazinopropionic acid, taurine, D,L-ornithine, or sulphanilamine which potentiates the inhibitory action of GABA,

inositol 1,4,5-triphosphate,

guanosine 5' cyclic monophosphate or 8-bromo guanosine 5' cyclic monophosphate which relaxes smooth muscle,

an inhibitor of the uptake system for glycine, the inhibitory synaptic transmitter of the spinal cord, such as hydrazinoacetic acid,

isoquinoline-sulfonamide inhibitor of protein kinase C, cAMP-dependant protein kinase, or cGMP-dependent protein kinase such as N-(2-aminoethyl)-5-isoquinoline-sulfonamide,

Ribavirin which is active against HSV-1 and 2, hepatitis, and influenza viruses, or phosphonoacetic acid which is a highly specific inhibitor of Herpes Simplex virus induced polymerase and is active against HSV-1 and HSV-2, or adenine arabinoside (ara-A), cytosine arabinoside (Ara-C), ara-A 5'-monophosphate (ara-AMP), or hypoxanthine arabinoside (ara-Hx) which is active against HSV or phagycin which is active against vaccinia and HSV, or 4-fluoroimidazole, 4-fluoroimidazole-5-carboxylic acid, 4-fluoroimidazole-5-carboxamide, 5-fluoro-1-B-D-ribofuranosylimidazole-4-carboxamide, 5-amino-1-B-D-ribofuranosylimidazole-4-carboxamide, poly (I), poly (C), sinefungin, iododeoxyuridine, 9-(2-hydroxyethoxymethyl) guanine, gliotoxin, distamycin A, netropsin, congocidine, cordycepin, 1-B-D-arabinofuranosylthymine, 5,6-di-hydroxy-5-azathymidine, pyrazofurin, toyocamycin, or tunicamycin,

an inhibitor of fungal chitin synthetase such as polyoxin D, nikko-mycin Z, or nikkomycin X,

an impermeant antifungal agent such as ezomycin A₁, A₂, B₁, B₂, C₁, C₂, D₁, or D₂ or platenocidin, septacidin, sinefungin, A9145A, A9145C, or thraustomycin,

an inhibitor of central nervous system carbonic anhydrase such as methazolamide, or 2-benzoylimino-3-methyl- \square^4 -1,3,4-thiadiazoline-5-sulfonamide substituted at the benzoyl group with 3,4,5-trimethoxy, 2,4,6-trimethoxy, 2,4,5-trimethoxy, 4-chloro, 4-bromo, 4-iodo, or hydrogen,

an inhibitor of dopamine-B-hydroxylase during the synthesis of norepinephrine and epinephrine such as fuscic acid, 5-(3',4'-dibromobutyl)picolinic acid, 5-(3'-bromobutyl)

picolinic acid, 5-(3',4'-dichlorobutyl)picolinic acid, YP-279, benzyloxyamine, p-hydroxybenzyloxyamine, U-21,179, U-7231, U-6324, U-0228, U-5227, U-10,631, U-10,157, U-1238, U-19,963, U-19,461, U-6628, U-20,757, U-19,440, U-15,957, U-7130, U-14,624, U-22,996, U-15,030, U-19,571, U-18,305, U-17,086, U-7726, dimethyldithiocarbamate, diethyldithiocarbamate, ethyldithiocarbamate, 2-mercaptoethylguanidine, thiophenol, 2-mercaptoethylamine, 3-mercaptopropylguanidine, 3-mercaptoethyl-N-methylguanidine, 2-mercaptoethanol, 2-mercaptoethyl-N-methylguanidine, 2-mercaptoethyl-N,N'-dimethylguanidine, 4,4,6-trimethyl-3,4-dihydropyrimidine-2-thiol, N-phenyl-N'-3-(4H-1,2,4-triazolyl)thiourea, methylspinazarin, 6,7-dimethylspinazarin, 7-O-methylspinochrome B, 6-(3-hydroxybutyl)-7-O-methylspinachrome B, aquayamycin, chrothiomycin, frenoclicin, N-n-butyl-N'-3-(4H-1,2,4-triazolyl)thiourea, propylthiouracil, mimosine, mimosinamine, or mimosinic acid,

an inhibitor of histidine decarboxylation during the synthesis of histamine such as 2-hydroxy-5-carbomethoxybenzyloxyamine, 4-toluene-sulfonic acid hydrazide, 3-hydroxybenzyloxyamine, hydroxylamine, aminooxyacetic acid, 4-bromo-3-hydroxybenzyloxyamine (NSD-1055), rhodanine substituted in the 3 position with p-chlorophenethyl, p-chlorobenzyl, p-methylthiobenzyl, p-methylbenzyl, p-fluorobenzyl, amino, 3,4-dichlorobenzyl, p-bromobenzyl, p-methoxybenzyl, p-bromoanilino, p-iodoanilino, p-chloroanilino, p-toluidino, anilino, 2,5-dichloroanilino, dimethylamino, or p-methoxyphenyl; 2-mercaptobenzimidazole-1,3-dimethylol, 4-bromo-3-hydroxybenzoic acid, 4-bromo-3-hydroxybenzyl alcohol, 4-bromo-3-hydroxyhippuric acid, (R,S)- α -fluoromethyl-histidine, (S)- α -fluoromethylester, L-histidine ethyl ester, L-histidinamide, D,L-3-amino-4-(4-imidazolyl)-2-butanone, 2-bromo-3-hydroxybenzyloxyamine, 5-bromo-3-hydroxybenzyloxyamine, 4,6-dibromo-3-hydroxybenzyloxyamine, aminooxypropionic acid, benzyloxyamine, 4-bromo-3-benzenesulfonyloxybenzyloxyamine, 3',5,7-trihydroxy-4',6-dimethoxyisoflavone, lecanoric acid, N-(2,4-dihydroxybenzoyl)-4-aminosalicylic acid, or 3',5,7-trihydroxy-4',8-dimethoxyisoflavone,

~~an pharmaceutical agent of drug that appear in Physicians Desk Reference, Edward R. Barnhart, 41th ed., 1987, Medical Economics Company Inc., N.J.; USAN and the Dictionary of Drug Names, ed. by Mary C. Griffiths, The United States Pharmacopiedial Convention, (1986); and The Pharmacological Basis of Therapeutics, ed. by A.G. Gilman, L. Goodman, A. Gilman, 7th ed., (1985), MacMillan Publishing Co., N.Y., N.Y.,~~

a centrally acting converting enzyme inhibitor such as captopril,

an antibacterial agent such as penicillin, cephalosporin, or cephamycin, with β -lactamase resistance,

an agent which blocks bacterial synthesis of tetrahydrofolate such as a sulfonamide, ~~(an analogue of p-aminobenzoic acid)~~ including sulfanilamide, sulfadiazine, sulfamethoxazole, sulfisoxazole, or sulfacetamide,

an inhibitor of dihydrofolate reductase including pyrimethamine, cycloguanil, trimethoprin, isoaminopterin, 9-oxofolic acid, or isofolic acid,

a bactericidal agent such as nalidixic acid or oxolinic acid,

an inhibitor of bacterial protein synthesis such as vancomycin, an aminoglycoside, erythromycin, tetracyclin, or chloramphenicol,

an inhibitor of viral DNA polymerase such as vidarabine,

tuberculostatic or tuberculocidal agent such as isoniazid or aminosalicylic acid,

an anthelmintic agent such as oxamniquine, piperazine, metronidazole, diethylcarbamazine, paromomycin, niclosamide, bithionol, metrifonate, hycanthone, dichlorophen, or niclosamide,

an H₂-blocking agent such as cimetidine or ranitidine,

an agent which blocks release of norepinephrine such as sotalol, guanethidine, pindolol, pronethalol, KO 592, practolol, oxprenolol, or pronethalol,

a xanthine oxidase inhibitor such as allopurinol, thioinosinate, 5,7-dihydroxypyrazolo 1,5-pyrimidine substituted at the 3 position with hydrogen, nitro, bromo, chloro, phenyl, 3-pyridyl, p-bromophenyl, p-chlorophenyl, p-acetylanilino, p-tolulyl, m-tolulyl, naphthyl, or 3,4-methylenedioxyphenyl; 8-(m-bromoacetamidobenzylthio)hypoxanthine, 8-(m-bromoacetamidobenzylthio)hypoxanthine, guanine substituted at the 9 position with phenyl, 4-chlorophenyl, 3-chlorophenyl, 3,4-dichlorophenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, 4-dimethylaminophenyl, 4-aminophenyl, 3-aminophenyl, 3-trifluoromethylphenyl, 4-benzamido, 4-carboxylphenyl, 4-methylphenyl, 4-ethylphenyl, 3-methylphenyl, B-naphthyl, or 4-ethoxyphenyl; 4,6-dihydroxypyrazolo 3,4-d pyrimidine, 4-trifluoromethylimidazoles substituted at the 2 position with phenyl, p-chlorophenyl, p-methoxyphenyl, p-acetylanilino, p-nitrophenyl, p-dimethylaminophenyl, p-cyanophenyl, p-fluorophenyl, p-carboxyphenyl, m-chlorophenyl, 3,4-dichlorophenyl, 4-pyridyl, 3-pyridyl, 2-quinolyl, 6-quinolyl, 4-quinolyl, 7-quinolyl, 2-pyrazinyl, or 1-(2-pyridyl-4-trifluoromethyl-5-bromoimidazolyl; 5-(4-pyridyl)-1,2,4-triazoles substituted at the 5 position with 4-pyridyl, 3-pyridyl, 2-pyridyl, phenyl, p-chlorophenyl, m-chlorophenyl, p-sulfonamidophenyl, 3,5-dichlorophenyl, 3,5-dicarboxyphenyl, 6-quinolyl, 2-furyl, 4-pyridazinyl, 2-thienyl, 2-pyrimidinyl, 4-pyrimidinyl, or 4-pyrazinyl; difunisal, 4(or 5)-(2-aminoethylthio-azo)imidazole-5(or 4)-carboxamide, 4 (or 5)-diazimidazole-5(or 4)-carboxamide, or S-δ5(or 4)-carbamoyl-4(or 5)-imidazolyl azo cysteine,

an agent which inhibits DNA synthesis such as a bis-thiosemicarbazone, 3,5-diisopropylsalicyl-hydroxamic acid, 4-hydroxybenzoylhydroxamic acid, 3-methylsalicylhydroxamic acid 2,5-dihydroxybenzoylhydroxamic acid, or 2-hydroxy-3,4,5-trimethoxybenzoylhydroxamic acid; or which inhibits nucleotide synthesis such as N-(phosphoacetyl)-L-aspartate which inhibits asparatase transcarbamylase during pyrimidine

synthesis, or azaserine or 6-diazo-5-oxo-L-norleucine which inhibits purine synthesis at the phosphoribosyl-formyl-glycineamidase synthetase step; or which is an antifolate such as methotrexate, 2,4-diamino-5-benzyl-6-(4-phenylbutyl) pyrimidine, 2,4-diamino-5-phenyl-6-(4-phenylbutyl) pyrimidine, 2,4-diamino-5-phenyl-6-(3-anilinopropyl) pyrimidine, 2-amino-4-hydroxy-5-phenyl-6-(3-p-aminobenzoylglutamic acid propyl) pyrimidine, N-(p-oo(2,4-diamino-6-quinazolinyl)methyl-methylamino- benzoyl-L-glutamic acid, N-p-2,4-diamino-5-methylquinazolinyl)methylaminobenzoyl-L-aspartic acid, N-p-(2-amino-4-hydroxy-6-quinazolinyl) methyl-methylamino benzoyl-L-glutamic acid, 2,4-diaminoquinazolines: CCNSC 105952, CCNSC 112846, CCNSC 121346, CCNSC 122761, CCNSC 122870, CCNSC 529859, CCNSC 529860, or CCNSC 529861; 8-aza GMP, 7-deaza-8-aza GMP, 2'-dGMP, B-D-arabinosyl GMP, pentopyranine A-G, B-ribofuranosyl-1,3-oxazine-2,4-dione, pyrazofurin, 6-(p-chloroacetylanilinomethyl)-5-cetylvinylanilinomethyl)-5-(p-chlorophen yl)-2,4-diaminopyridine, 6-(p-chloroacetyl- ethylanilino-methyl)-5-(p-chlorophenyl)-2,4-diamino pyridine, 6-(p-chlorophenylbutylanilinomethyl)-5-(p-chlorophenyl)-2,4-diamino pyridine, p-(2,6-diamino-1,2-dihydro-2, 2-dimethyl- S-triazin-1-yl) phenylpropionyl sulfanilylfluoride or variants of the propionamide bridge of acrylamido, N-ethylsulfonamido, N-ethylcaboxamido, oxyacetamido, or oxythyloxy; or which inhibits purine or pyrimidine synthesis such as xylosyladenine, 6-azauridine, 5-aminouridine, 5-azauric acid; or which inhibits nucleotide interconversion such as hadacidin, 6-mercaptopurine, azathioprine, nitro-dUMP, psicofuranine, decoyinine, 5-fluorouracil, 5-fluorodeoxyuridine, shadowmycin; or which inhibits nucleotide utilization such as cytosine arabinoside, arabinosyladenine; or which becomes incorporated into polynucleotides such as 8-azaguanine, tubercidine, toyocamycin, sangivamycin, formycin, 7-deazainosine, 8-azainosine, or 7-thia-7, 9-dideazainosine; or which is a glyoxalase inhibitor such as Glyo-I, or Glyo-II,

an agent which blocks synthesis of prostaglandin A₂ which effects platelet aggregation such as salicylic acid, pyrogallol, 5,8,11,14-eicosatetraenoic acid, □-naphthol, guaiacol, propylgallate, nordihydroguaiaretic acid, N-0164, benzydamine, 9,11-azoprostanoic acid, 13-dienoic acid, 2-isopropyl-3-nicotinylindole,

an agent which blocks prostaglandin synthetase such as indomethacin, sulindac, tolmetin, mefenamic acid, ibuprofen, naproxen, fenoprofen, flurbiprofen, ketoprofen, meclofenamic acid, flufenamic acid, niflumic acid, benzydamine, oxyphenbutazone, aspirin, acetaminophen, salicylamide, O-carboxydiphenylamine, tolectin, diclofenac, 2,7-dihydroxynaphthalene, 5-(4-chlorobenzoyl)-1-methylpyrrole-2-acetic acid, 5-(4-methylbenzoyl)-1,4-dimethylpyrrole-2-acetic acid, 5-(4-chlorobenzoyl)-1,4-dimethylpyrrole-2-acetic acid, 5-(4-fluorobenzoyl)-1,4-dimethylpyrrole-2-acetic acid, 5-(4-chlorobenzoyl)-1,4-dimethylpyrrole-2-(2-propionic acid), 5,6-dehydroarachidonate, 11,12-dehydroarachidonate, or 5,8,11,14-eicosatetraenoate; or of an

agent which blocks lipooxygenase or blocks leukotriene action such as BW755C, FPL 55712, or U-60,257,

an antiarrhythmic agent such as procainamide or quinidine,

an inhibitor of hepatic synthesis of Vitamin K dependent clotting factors such as warfarin sodium, dicumarol, 4-hydroxycoumarin, phenprocoumon, or acenocoumarol,

an agent which relaxes vascular smooth muscle such as hydralazine, minoxidil, or isoxsuprine,

Na⁺ K⁺ -ATPase inhibitor such as digitoxigenin, digoxigenin, cymarol, periplogenin, or strophanthidiol, or ouabain glycosides, cardenolides, or basic esters, or ICI-63,632, ICI-63,605, ICI-62,655, ICI-62,838, ICI-69,654, ICI-58,622, ICI-61,374, ICI-57,267, ICI-61,424, ICI-61,411, ICI-65,199, ICI-70,898, ICI-70,899, ICI-70,900, ICI-70,901, ICI-62,966, ICI-65,210, ICI-63,116, ICI-62,936, ICI-65,551, ICI-63,978, ICI-62,276, ICI-63,056, ICI-67,135, ICI-67,167, ICI-67,134, ICI-67,875, ICI-67,880, or ICI-61,558,

a calcium channel blocker such as prenylamine, verapamil, fendiline, gallopamil, cinnarizine, tiapamil, diltiazem, bencyclan, or nifedipine; or an agent which stabilizes calcium binding to cellular calcium stores and thereby inhibits the release of this calcium by contractile stimuli such as 8-(N,N-diethylamino)-octyl 3,4,5-trimethoxybenzoate (TMB-8),

a monoamine oxidase inhibitor such as tranlycypromine, phenylethylamine, trans-cinnamic acid, phenelzine, or isocarboxazid,

a benzodiazepine compound such as clorazepate,

valproic acid,

an agent which causes repression of the synthesis of HMG-CoA reductase such as 20- Δ -hydroxycholesterol, 22-ketocholesterol, 22- Δ -hydroxycholesterol, 25-hydroxycholesterol, 22- Δ -hydroxycholesterol, 7- Δ -hydroxycholesterol, 7- Δ -hydroxycholesterol, 7-ketocholesterol, or kryptogenin; or of an agent which inhibits HMG-CoA reductase such as, lorelco; or of an agent which inhibits lipolysis such as 5-methylpyrazole -3-carboxylic acid (U-19425), nicotinic acid, uridine, inosine, 3,5-dimethylisoxazole (U-21221), 3,5-dimethylpyrazole, prostaglandin E₂, eritadenine, or eritadenine isoamyl ester; or of an agent which inhibits lipogenesis such as ascofuranone, (-)-hydroxycitrate, or tetrolyl-CoA; or of an agent which is hypocholesterolemic such as lentysine; or of an agent which lowers triglycerides such as lipid; or of an agent which is an inhibitor of acetyl-CoA carboxylase during lipogenesis such as 2-methyl -2-p-(1,2,3,4-tetrahydro-1-naphthyl)-phenoxy-propionate (SU13437), 2-(p-chlorophenoxy)-2-methylpropionate, kynurenate, xanthurenate, kynurenine, 3-hydroxyanthranilate, or 2-methyl-2-p-(p-chlorophenyl)phenoxypropionate; or of an agent which is an inhibitor of hepatic Δ -lipoprotein production such as orotic acid,

a vasodilator such as WS-1228A, or WS-1228B; or of an anti-inflammatory agent such as

amicomacin A,

a protease inhibitor such as leupeptin; or which is an inhibitor of pepsin such as a pepstatin, a pepstanone, or a hydroxyepstatin,

an inhibitor of cell surface enzymes such as bestatin, amastatin, forphenicine, ebelactone, or forphenicin,

a phosphodiesterase inhibitor such as theophyllineacetic acid, theophylline, dyphylline, disodium cromoglycate, 6-n-butyl-2,8-dicarboxy-4,10-dioxo-1,4,7,10-tetrahydro-1,7-phenanthrolin, 2-chloroadenosine, dipyridamole, EG 626, AY-17,605, AY-17,611, AY-22,252, AY-22,241, cis-hinokiresinol, oxy-cis-hinokiresinol, tetrahydro-cis- hinokiresinol, trans-hinokiresinol, dehydrodicaffeic acid, 2,6,4'-trihydroxy-4-methoxybenzophenone, p-hydroxyphenyl crotonic acid, papaverine, 3-(5-tetrazolyl)-thioxanthone-10,10-dioxide, 3-carboxythioxanthone-10,10-dioxide, W-7, HA-558, MY-5445, OPC-3689, OPC-13135, or OPC-13013, reticulol, PDE-I, or PDE-II,

an inhibitor of tyrosine hydroxylase, the enzyme catalyzing the rate-limiting reaction in the biosynthesis of norepinephrine, such as azadopamine, isopropylazadopamine, dimethylazadopamine; triphenolic compounds such as n-propylgallate; diphenolic benzoic acid, ~~derivatives such as~~ 3,4-dihydroxybenzoic acid; phenylcarbonyl, ~~derivatives such as~~ 3,4-dihydroxybenzaldehyde, arterenone, or adrenalone H 22/54, 3-iodo-L-tyrosine, D,L-□-methyl-p-tyrosine, L-3-iodo-□-methyltyrosine, 3-bromo-□-methyltyrosine, gentistic acid, 3-chloro-□-methyltyrosine, phenylalanine ~~derivatives~~, 3,5-diiodo- L-tyrosine, 3,5-dibromo-L-tyrosine, 3-bromo-□-methyl-L- tyrosine, 3-fluro-□-methyl-L-tyrosine, ~~catechol analogues~~, 3,4-dihydroxyphenylethylacetamide, 3,4-dihydroxyphenyliso- propylacetamide, 3,4-dihydroxyphenylbutylacetamide, 3,4-di-hydroxyphenylisobutylacetamide, D,L-□-methylphenylalanine, D,L-3-iodophenylalanine, D,L-4-iodophenylalanine, D,L-□-methyl-3-iodophenylalanine, D,L-a-methyl-3-bromophenylalanine, D,L-□-methyl-3-chlorophenylalanine, D,L-□-methyl-3-fluorophenylalanine, mimosine, mimosinamine, mimosinic acid, 7-O-methylspinochrome B, 6-(3-hydroxybutyl)-7-O-methylspinachrome B, aquayamycin, chrothiomycin, frenolicin, fuscic acid, pentylpicolinic acid, dopstatin, methylspinazarin, 6,7-dihydroxymethylspinazarin, 3-ethyl-□-methyltyrosine, 3-methyl-□-methyltyrosine, 3-isopropyl-x-methyltyrosine, 3-allyl-□-methyltyrosine, 3-4-hydroxy-3-(2-methylallyl)-phenyl-2-methylalanine, 3-3-(2,3-epoxypropyl)-4-hydroxyphenyl-2-methylalanine, 3-isobutyl-□-methyltyrosine, 3-methylvinyl-□-methyltyrosine, 5-methyl-6,7-diphenyltetrahydropterin, 3-(2,3-dihydro-2,2-dimethyl-5-benzofuranyl-2-methylalanine, 3-2,3-dihydro-2,2-dimethyl-5-benzofuranyl-2-methylalanine, □-methyldopa, or ethyl-3-amino-4H-pyrrolo 3,4-isoxazole carboxylate, and

proteins including enzymes and hormones such as insulin, erythropoietin, interleuken 2,

interferon, growth hormone, atrial natriuretic factor, tissue plasminogen activator.

229. (Previously Presented) The method according to claim 1, wherein the phthalhydrazide comprises at least one selected from the group consisting of phthalimide, aminophthalic acid diester, aminophthalic acid dihydrazide, aminophthalic anhydride and phthalhydrazide protected by a hydrolyzable group.